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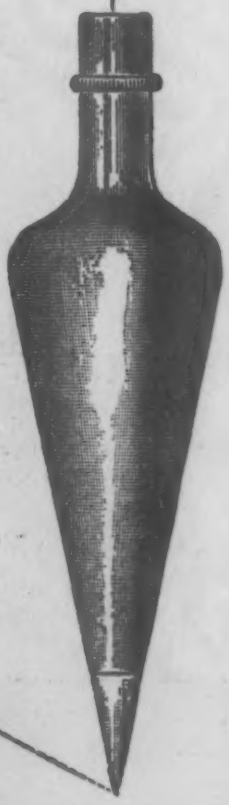

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RESTORATIVE ENDOANEURYSMORRHAPHY BY VEIN GRAFT INLAY*

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NEW YORK, N. Y.

IT WAS NEARLY FIFTY YEARS AGO that Dr. Rudolph Matas[1] introduced the surgical terms restorative and reconstructive endoaneurysmorrhaphy. More than 50 years have elapsed since he demonstrated to the profession that gangrene may be regularly avoided by employing his technic of obliterative endoaneurysmorrhaphy for the cure of aneurysm of the extremities. Though Doctor Matas early recognized the advantage of maintaining a pulsating arterial blood flow to the affected extremity for a complete restitution of function, his restorative technic clearly demonstrates that the attempt is made not at the expense of important collateral vessels—the salient feature of all his technics is the preservation of collateral vessels through an intra-saccular approach.

It is my wish to present a technic of vein graft inlay for the repair of degenerative arterial aneurysm with restoration of blood flow which conserves the principle of minimal damage to collateral vessels.

METHOD

A generous skin incision affording free access to the proximal and distal poles of the aneurysm is made; the edges of the skin are covered with towels held in place by Michel clips. Following the securing of hemostasis, gloves and instruments are changed before proceeding with the operation. Time may be conserved by having an assistant proceed with the removal of a segment of vein for use as a graft—preferably from another extremity. The superficial femoral vein is most commonly used. An incision of the fascia is made directly over the aneurysm. The afferent artery can usually be located by palpating the pulse and identified by blunt dissection staying close to the upper pole of the aneurysm sac. A double turn of vaselinized umbilical tape serves well for temporary occlusion of the artery. Should a sizable collateral branch arise at or very near the artery-aneurysm junction, this may be separately

* Read before the American Surgical Association, March 25, 26 and 27, Hot Springs, Virginia.

controlled with a double turn of heavy silk. The efferent parent artery is likewise identified and controlled.

The aneurysm sac is then opened widely from pole to pole following securing of the parent artery by tapes or rubber shod clamps. The clot is quickly evacuated and a search is made for the openings of vessels within the sac. All vessel openings exclusive of the parent artery openings are sutured with three zero Deknatel silk from within the sac. Next, the distance between the parent artery openings within the sac is measured. To this measurement add four centimeters for the correct length of the vein graft to be used to bridge the arterial defect.

Vitallium tubes, as recommended in a non-suture method for vein graft bridging of arterial defects[2] serve as a prosthesis for retention of the vein graft inlay. Figure 1 illustrates the vitallium tubes and the method of mounting a tube on either end of the vein graft.[4, 5, 6] The everted vein is held in place by a four zero Deknatel silk ligature placed around the tube behind a tying (holding) ridge on the tube.

Figure 2A illustrates an aneurysm with the sac open to show the parent artery openings. Two smaller openings are likewise indicated. Rubber shod clamps to control blood flow are illustrated. The size of the openings of the parent artery indicate the size of the vitallium tubes to be employed. In some cases of large aneurysm the openings are far apart and it may be necessary to employ a vitallium tube one millimeter smaller for the distal opening. On the other hand, it is fortunate that usually the openings are larger in diameter than the parent artery. This enables the operator to introduce with ease larger vein mounted tubes than would be possible if the parent artery were severed from the aneurysm.

Figure 2B illustrates the vein graft inlay in place. The retaining sutures of zero Deknatel silk are placed around the vein mounted vitallium tubes so that when tied tightly with a surgeon's knot the ligature falls behind the holding ridges on the tubes. The sutures of finer (three zero) Deknatel silk placed near the ends of the vitallium tubes are tied, just snug, to coapt the vein and artery intimas. Some care must be employed both in the accurate placement of these sutures and the avoidance of a contiguous nerve or vein in case, as sometimes happens, part of the suture may be extra-saccular.

On account of vein valves, the proximal end of the vein graft should, of course, be joined with the distal artery opening.

Figure 2C shows the retaining ligatures tied, the parent artery deoccluded and sutures placed in the sac wall which, when tied, will cover the vein graft. It is important at this stage of the operation to make sure that any air bubbles within the vein graft are made to pass on by pressure upon the graft or elevation of the extremity.

Figure 2D illustrates the vein graft covered and additional sutures placed for imbricating the aneurysm sac. Silk technic is employed throughout and the wound is closed without drainage.

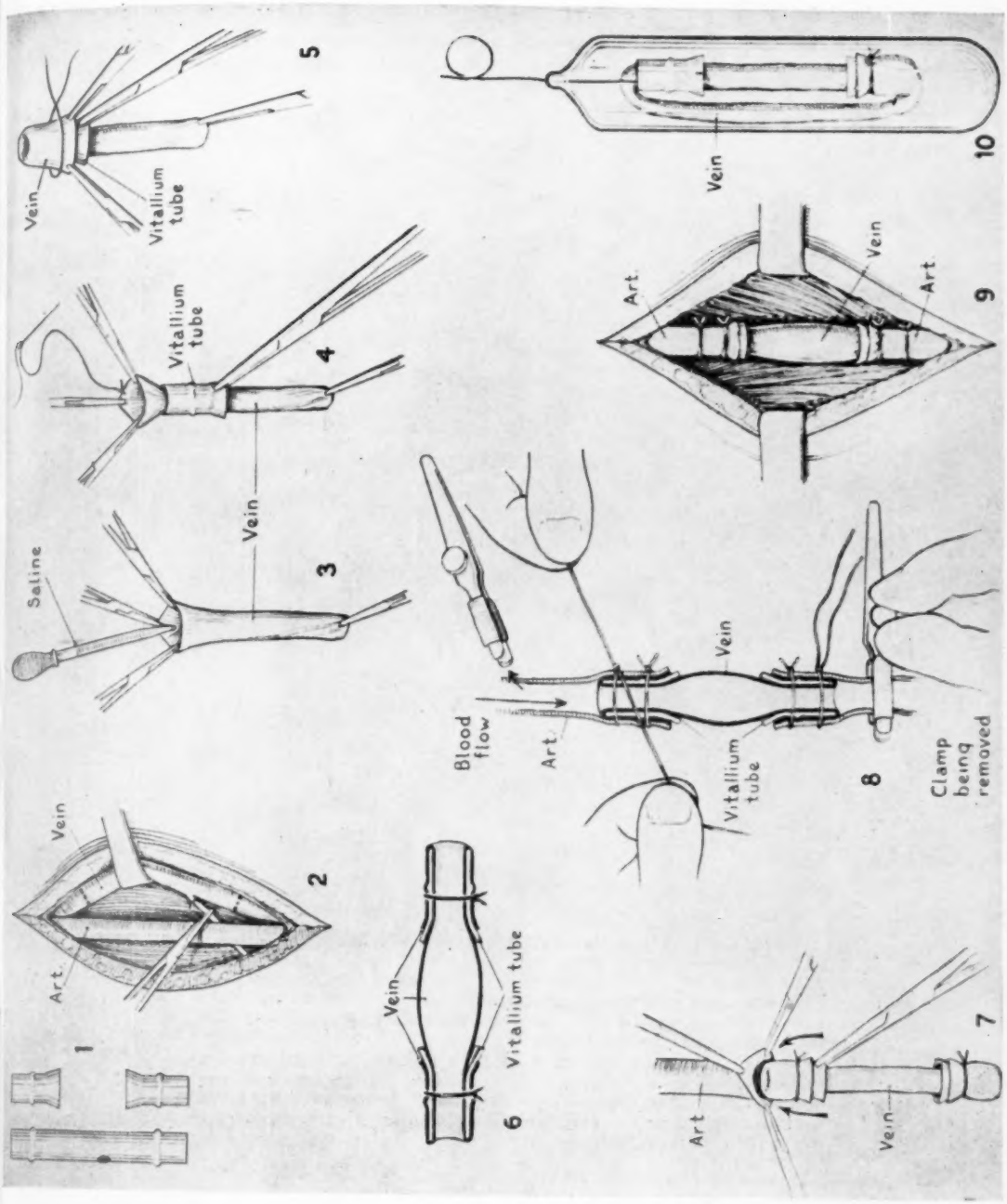

FIG. 1.—Drawings to illustrate different stages in the nonsuture technique. (1) (right) Vitallium tubes employed in the double tube nonsuture technique. (2) A vein graft branch ligated flush and clamped distally before being cut. (3, 4 and 5) The method of mounting the vein graft upon the tube. (6) A vein graft ready for use.

CASE REPORTS

Case 1.—A 42-year-old colored male entered the Presbyterian Hospital May 27, 1945, complaining of a pulsating swelling in the right thigh of 2½ years duration. His

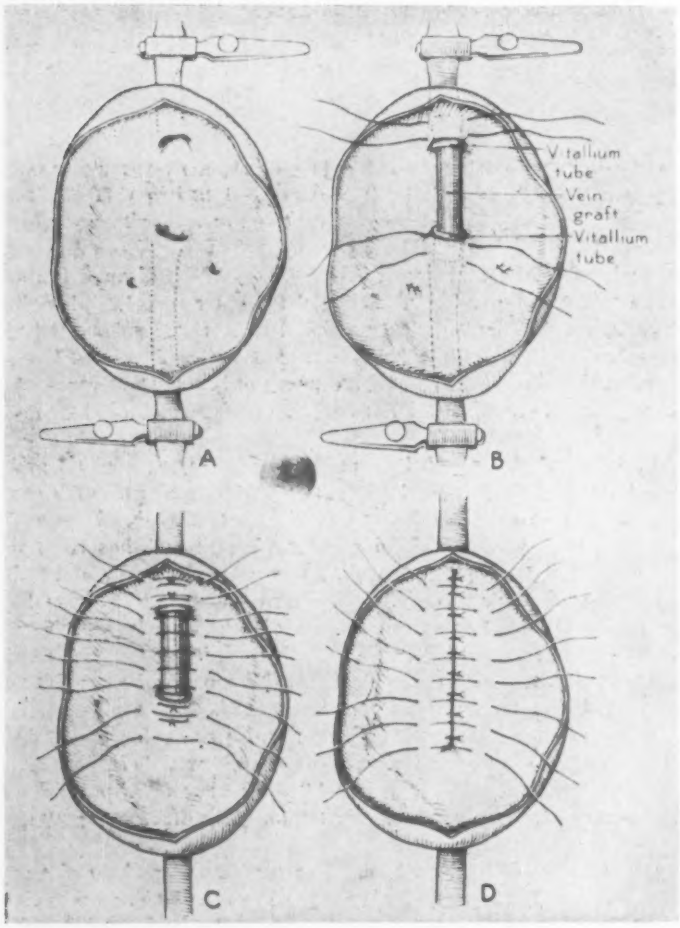

FIG. 2.—(A) An aneurysm with the sac incised to show the parent artery openings and other branch openings. (B) The vein graft with a vitallium tube on either end cannulating the proximal and distal orifices of the parent artery. The proximal holding suture ligatures of heavy silk and the distal suture ligatures of finer silk for coapting vein intima to artery intima are shown in place ready to be tied. (C) The vein graft with the suture ligatures about the tubes tied. Note the rubber shod clamps have been removed permitting the anastomosis to function at this stage. Sutures are layed for covering the graft. (D) The first row of sutures tied covering the graft with a second row layed.

past history was given as follows: Penile lesion in 1923. In 1926 the patient received 100 intravenous and 70 intramuscular injections because of the presence of a positive Wassermann. In 1934 the Wassermann was still positive but became negative following another series of treatments for syphilis over a 3-year period. In 1940 the patient received

a bullet wound over the anterior aspect of the right thigh. Two and one-half years later a pulsating swelling developed on the medial aspect of the thigh.

Examination: Presenting on the medial aspect of the right thigh, lower middle third, was noted a pulsating swelling the size of a large grapefruit. At the same level, over the anterior aspect of the thigh, a round scar one centimeter in diameter was present. Auscultation revealed the presence of a systolic murmur over the tumor. The superficial veins below the knee were engorged. One could not be sure of feeling pulsation over the posterior tibial artery on the right. Pulsation over the dorsalis pedis artery on the right were faint in comparison with the left.

FIG. 3.—An arteriogram of the femoral artery in Case 1. Note the vitallium tubes with the intervening vein graft. Slight angulation at the proximal end suggests that the vein graft is a little redundant.

On May 31, 1945, the aneurysm was operated upon through an intra-saccular approach. The defect in the femoral artery was bridged with a vein graft bearing a 5 mm. vitallium tube on either end. Wound healing following operation was by primary intention. No observer could feel a pulsation over the posterior tibial artery postoperatively. Some thought a faint pulsation was detected on different occasions over the right dorsalis pedis artery but there was no full agreement on this point. However, the oscillometric readings from the lower 1/3 of the right leg were ½ division consistently and the patency of the anastomosis was confirmed by arteriogram on the 11th postoperative day.

Figure 3 shows an arteriogram of the femoral artery (Case 1) showing the vein

graft anastomosis and the vitallium tubes in place. The angulation of the vein graft suggests some redundancy.

Follow-up: The patient was examined on follow up visits 3 mos., 6 mos., 12 and 22 mos. postoperatively. The man has had complete exercise tolerance. The reports on being able to palpate a pulsation in the dorsalis pedis artery on the right have varied much as obtained in the early postoperative days previous to arteriographic demonstration of the patency of the anastomosis. The oscillometric readings at 22 mos. follow up was ½ division on lower 1/3 of leg—the same as during the early postoperative days.

Case 2.—A 39-year-old Italian woman who was admitted to the Presbyterian Hospital October 29, 1945, complaining of a pulsating swelling in the left groin of 18 months' duration. This patient had suffered from rheumatic heart disease dating back to an attack of rheumatic fever at age five.

The present illness began in April 1944 with fever, malaise and loss in weight. One day pain in the left groin suddenly appeared, accompanied by a pulsating swelling. The pain gradually subsided over a two-week period. Finally, some months later, the patient was diagnosed as having streptococcus viridans endocarditis with a mycotic aneurysm of the left femoral artery. The infection was cured with penicillin therapy in September 1944, but the aneurysm continued to grow. After the aneurysm had been present one year (some six months before admission) symptoms of intermittent claudication in the left leg appeared.

Operation: (Nov. 23, 1945) Exploration revealed a saccular aneurysm of the common femoral artery with fibrotic occlusion of the distal opening. The latter finding explained the recent history of intermittent claudication and the absence of palpable pulsations over the posterior tibial and dorsalis pedis arteries in this case.

The defect in the femoral artery was bridged with a graft taken from the right superficial femoral vein. The proximal opening of the artery was intubated with a 5 mm. vitallium tube bearing the cuffed vein. It was necessary to slit the distal opening 1 cm. to get beyond the area of fibrotic occlusion. Even though the femoral artery was badly contracted at this point it was possible to introduce a 4 mm. vitallium tube mounted on the other end of the vein graft. When the femoral artery was deoccluded proximally and distally, a substantial pulse was palpable in the artery distal to the anastomosis.

Follow-up oscillometric readings on this patient from the distal 1/3 of the leg immediately following operation were up to ¼ division.

On the 13th postoperative day an arteriogram confirmed the patency of the anastomosis.

Oscillometric readings have been maintained at ¼ division from the distal 1/3 of the leg in this case now in excess of one year since operation. She is free of symptoms of circulatory insufficiency in the leg.

Case 3.—A 68-year-old man who was admitted to the Presbyterian Hospital September 5, 1946, because of swelling of the right leg, pain and swelling behind the knee of eight months' duration. For some two years the patient had had transient pains in the calf of the right leg upon exercise. The swelling and pain in the popliteal space had grown progressively worse over the eight months' period prior to admission. For three months prior to admission the leg below the knee had become greatly swollen.

Examination: The right leg was considerably larger than the left. The surface veins were engorged. Occupying the entire popliteal space was a pulsating mass over which one could hear a systolic murmur. Pulsations in the right dorsalis pedis and posterior tibial arteries were less prominent than on the left. Oscillometric readings from the upper third of the right (affected) leg (2½ div.) were approximately two thirds of those from the left leg. There was evidence of arteriosclerosis. The Wassermann test was negative.

Operation September 12, 1946, revealed an arteriosclerotic fusiform aneurysm of the right popliteal artery which measured 18 centimeters in length. The parent artery above and below the aneurysm was controlled by tapes. The aneurysm sac was opened,

clot evacuated and small vessel openings sutured. Finally a femoral vein graft from the left leg mounted on two 8 mm. tubes was introduced to bridge the arterial defect within the sac and the sac was closed over the graft.

Following operation the oscillometric readings from the upper 1/3 of the right leg approximated those from the left leg representing an increase of 35 per cent above the preoperative level. Pulsations in the right foot arteries were increased equal to those on the left by palpation.

Follow-up: At four and six mos. respectively, following operation oscillometric readings from the two legs have remained equal (2½). Pulsation can be palpated throughout the vein graft. The man is active and free of symptoms of circulatory insufficiency in the right leg.

Figure 4 is an x-ray of the leg taken in the lateral position and shows the two vitallium tubes.

Case 4.—A 50-year-old colored man who was admitted to the Vanderbilt Clinic February 14, 1947, complaining of pain in the chest of four months' duration.

The patient gave a history of lues, insufficiently treated, in 1925. One and one-half years ago (1945) the patient was operated upon for an aneurysm of the right femoral artery. Since operation the patient has had to rest after walking four blocks on account of pain in the calf of the right leg.

Four months prior to admission the patient developed pain in the upper left chest followed by hoarseness two months later. There was a gradual loss of 12 lbs. in weight. He developed a non-productive cough and became short of breath on slight exertion.

Examination in the clinic revealed the presence of an aneurysm of the upper descending thoracic aorta. The Kline test was negative.

The patient was placed on bismuth therapy February 18, 1947. Shortly afterward he developed pain in the left popliteal region.

FIG. 4.—A lateral X-ray of the knee region of the leg in Case 3. Note the vitallium tubes and the presence of calcification in the wall of the artery proximal to the upper tube.

Upon admission to the Presbyterian Hospital on March 6, 1947, the patient was found to have a tender pulsating mass occupying the lower 2/3 of the left popliteal space. A loud systolic bruit was heard over the mass. There was distention of the superficial veins of the left leg below the knee. Pulsations in the left dorsalis pedis and posterior tibial arteries were good. The oscillometric readings from the lower 1/3 of the left leg at a pressure of 80 were two in comparison with ½ for the right leg at the same pressure and level. (The right femoral artery had been operated upon for aneurysm 1½ years before.)

The left leg was placed in extreme elevation. Large doses of codeine were required for the relief of pain. An alcoholic sympathetic ganglia block was done on 1, 2 and 3 left lumbar ganglia. A dry and warmer foot resulted.

On March 13, 1947, the popliteal aneurysm was operated upon. Through an intrasaccular approach a 10-centimeter vein graft, taken from the superficial femoral vein of the same leg was employed to bridge the defect in the lower popliteal artery. A 5 mm. vitallium tube was used to mount the vein graft proximally and a 4 mm. tube distally. A good pulsation was felt in the left dorsalis pedis artery at the conclusion of the

operation. On the day following operation the distal pulse remained good and the oscillometric reading from the lower 1/3 of the left leg was 1¼ divisions at a pressure of 80. On the third postoperative day the oscillometric readings are two divisions at 80 mm. pressure—representing a rise to the preoperative level. At 10 days postoperatively the wound is healing by primary intention and the oscillometric readings are being maintained.

DISCUSSION

There are some points of interest that would seem worth while discussing in connection with these four cases.

In Case 1, for example, all observers agreed to the absence of a palpable pulse over the posterior tibial artery following operation but agreed that, on occasion, a faint pulse could be detected over the dorsalis pedis artery. During the above convalescent period the presence of oscillometric readings of ½ division from the distal ⅓ of the leg was taken as strong evidence of patency of the anastomosis. This evidence was finally confirmed by arteriography.

Similarly, Case 2, the patient who for six months had had, upon exercise, symptoms of insufficient blood flow due to aneurysm with complete occlusion of the left common femoral artery, likewise had no certain palpable pulsations in the pedal arteries following a restorative operation. Again, as in Case 1, the oscillometer afforded dependable evidence (as confirmed by arteriography) of the status of the arterial anastomosis. The collateral circulation about the obstructed common femoral artery in this case before operation afforded an oscillometric reading that barely constituted a flicker of the needle. After restoration of blood flow by operation, an oscillometric reading of ¼ division from the distal ⅓ of the leg has been maintained.

It is granted there are factors affecting oscillometric readings such as degree of arteriosclerosis, vasomotor tone blood pressure, etc. That must be taken into consideration when comparing readings between different individuals. Due to the ages of Cases 1 and 2 it seems unlikely that arteriosclerosis is an important factor. In neither Case 1 or 2 had the vasomotor factor been neutralized by sympathetic interruption. Case 2 does have the low systolic blood pressure frequently encountered in rheumatic mitral disease.

Notwithstanding the above it is not unreasonable that the comparative differences in oscillometric readings between cases 1 and 2 is in the major part accounted for on the basis of the size and location of the arterial anastomoses. For example, considering the fact that readings were taken from the distal ⅓ of the leg in each case, it is but logical that the distance between the site of the anastomosis and the oscillometer plus the fact that the artery enlarges proximal-ward would, when in addition the size of the anastomosis is considered, greatly affect the magnitude of the oscillations. It is not surprising then that an anastomosis of the common femoral artery employing a 4 mm. vitallium tube, as in case 2, should yield an oscillometric reading of just half the magnitude of that afforded by a 5 mm. tube anastomosis of the superficial femoral at a more distal level, as obtained in case 1. Case 2, it may be recalled, registered an oscillometric reading of ¼ division in comparison with ½ division in case 1.

Of more importance, demonstrating the relatively greater effect the size of the vessel distal to the anastomosis has upon the magnitude of the oscillations, is the greater contrast with Case 4. A defect in the popliteal artery was bridged by a vein graft employing a 4 mm. tube on the distal end. In this case the anastomosis yielded an oscillometric reading of two divisions from the distal ⅓ of the leg. Other possible factors affecting the oscillometric readings in Case 4 is (1) the patient's age, (50 years)—some 10 years older than Cases 1 and 2. (2) Interruption of the sympathetic nerves to the extremity.

It is of further interest to state that analysis of the four cases operated upon employing the vein graft inlay technique revealed the salvage of all important collateral vessels.

CONCLUSION

The importance of restoring a pulsating arterial blood flow for the complete restitution of function in legs with damaged or diseased primary arteries was long ago emphasized by Matas[1] and Makins.[3] More recent evidence has been brought to bear on the subject by Bigger,[4] Maybury,[5] Freeman,[6] Heringman,[7] and the author.[2]

In the light of the above facts it is to the best interest of the patient to restore a pulsating arterial blood flow if it can be accomplished without damage to important collateral vessels.

Endoaneurysmorrhaphy employing a vein graft inlay restores a pulsating arterial blood flow without damage to important collateral vessels.

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THE "BORROWING-LENDING" HEMODYNAMIC PHENOMENON (HEMOMETAKINESIA) AND ITS THERAPEUTIC APPLICATION IN PERIPHERAL VASCULAR DISTURBANCES*

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IT IS NOW A WELL ESTABLISHED FACT that the volume of organs undergoes spontaneous, and even rhythmic, variations, primarily attributable to changes in the volume of the blood within the particular part. When more refined technics of plethysmography were developed, it became practical to carry out accurate quantitative studies of the fluctuations in volume in such peripheral parts as the pinnae, the fingers and the toes, and thus to secure much valuable information under normal resting conditions as well as in diseased states.

There are still numerous gaps in our knowledge of the precise nature of, and the numerous factors involved in, this mechanism, but certain facts have been established which not only have a fundamental physiologic significance but which also appear to have a definite bearing upon certain clinical conditions. It is the purpose of this communication to consider these facts as the basis of a concept which we have chosen to call the "borrowing-lending" phenomenon and for which we are suggesting the term hemometakinesia. We believe that this concept will provide a more rational approach than now exists toward the management of disturbances in the peripheral vascular circulation.

PLETHYSMOGRAPHY

The plethysmogram, which is the completed record of the plethysmograph, is essentially an ordinary type of Cartesian coordinate, with volume represented on the ordinate and time represented on the abscissa. It is thus a record of the changes in volume, in relation to time, of the particular part enclosed in the extremity cup. These recorded volume changes are the algebraic summation of many volume changes occurring in various degrees and directions in many different portions of the enclosed part.[1] Essentially, however, the changes in volume of the part represent changes in the volume of the vascular bed of the part.

Systematic studies with the plethysmograph have established the fact that small blood vessels in such peripheral parts as the pinnae, the fingers and the toes undergo spontaneous variation in volume. The resting individual, in a comfortable environment, presents at least five types of rhythmic changes in

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volume[1, 2] as follows: (1) pulse deflections, (2) respiratory deflections, (3) alpha deflections, (4) beta deflections, and (5) gamma deflections (Figs. 1–4). These changes which are conveniently (and arbitrarily) expressed as per 5 cc. of part, range in volume from less than 0.1 to 350 or more cu. mm.

Pulse Deflections.—Pulse deflections are obviously produced by the heart beat. They represent, in the main, the changes in volume of the part brought about by the blood delivered into the part with each heart beat (Fig. 1). The volume of the pulse deflections varies considerably, but in the normal resting individual the mean values have been found to be 6.9 cu. mm. in the tips of the fingers, 4.0 cu. mm. in the tips of the toes, and 4.1 cu. mm. in the pinnae.[2] The frequency of pulse deflection varies with the heart rate.

It is generally accepted that these changes in volume occur primarily within the arteries and arterioles, but it is believed that relatively large volume changes probably occur within the capillaries also, because of their number and total volume. It also seems likely that the veins and venules contribute to the pulse volume deflections. It is even possible that the volume changes within the arteriovenous anastomoses, capillaries, veins and venules in combination are of greater importance than those within the arteries and arterioles.

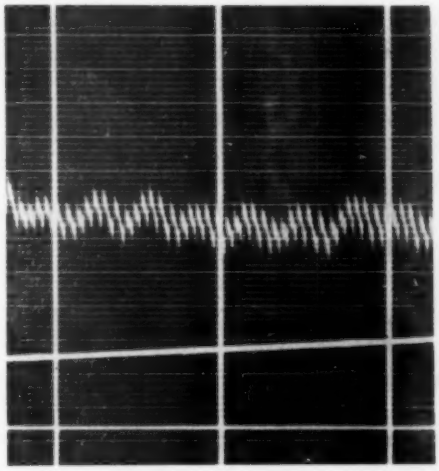

FIG. 1.—Plethysmogram of normal individual showing pulse deflections (reflecting the heart beats) and respiratory deflections which are represented by variations in the base line. Heavy white vertical lines indicate an elapsed time of 15 seconds.

Respiratory Deflections.—Respiratory deflections, which represent variations in volume occurring with the normal respiratory cycle, are most highly developed in the pinnae and least well developed in the toes (Fig. 1). Their volumes vary from less than 0.1 to 5 cu. mm. per 5 cc. of part.[2]

The respiratory deflection depends primarily upon the variations in the venous return to the heart brought about by respiration. Parallel with the increase in venous flow produced by inspiration there occurs a relatively rapid emptying of the venous blood from the part and a resultant decrease in its volume. With expiration, on the other hand, the relatively rapid rate of venous flow is retarded, and there is a resultant relative increase in the volume of the part.

Other factors possibly play a role in this mechanism, but too little is known about them at this time to warrant further comment. Of particular interest, however, is the special type of respiratory deflection which occurs in the fingers and toes immediately following a deep inspiration.[1, 2] There is first a spontaneous, sudden decrease in the volume of the part, varying from 5 to 105

cu. mm., and more prominent in the fingers than in the toes. At the same time the pulse deflections also show a decrease in volume. Shortly after these phenomena are observed, vasodilatation begins and continues until the previous pulsatile characteristics are resumed. Before vasodilatation is complete, however, a series of small alpha waves appear, varying from 2 to 8 cu. mm. After two or more successive deep inspirations, the extent of the response is progressively diminished until eventually a sort of tachyphylaxis occurs and vasoconstriction cease to appear. The volume change is lessened as the interval between inspirations is shortened. The volume change is not necessarily concordant; it may show either an increase or a decrease. Interestingly enough, it is not as definite, as predictable or as large in the pinnae as in the fingers and toes.

Alpha Deflections.—Alpha deflections, which occur less frequently than respiratory deflections, are usually smooth in contour, but are not uniform (Fig. 2). They vary in frequency and size, with a tendency toward an inverse relationship. The mean frequency has been found to be 7.9 per minute in the finger tips, 7.7 in the toes, and 8.6 in the pinnae,[2] and the mean volume for these respective parts has been found to be 14.5, 7.1 and 6.6 cu. mm.[2] Alpha deflections seem to vary from person to person, and even in the same person variations in the different peripheral parts are not necessarily concordant. Although they are independent of variations in arterial pressure,[3] these deflections are predominantly under the control of the sympathetic nervous system; they almost entirely disappear following interruption of sympathetic pathways.[2]

The volume changes represented by alpha deflections are due essentially to variations in volume of the blood within the part, but their frequency suggests the possibility that variations in lymph volume may be a contributing factor. The studies of Webb and Nicoll[4] on the bat's wing showed that contractions of the lymphatics are responsible for much of the flow of lymph, and McMaster's studies[5, 6] on other animals support these observations. Whether or not similar contractions occur in man is not known, but the frequency and rate of the lymphatic contractions observed in animals are of such a character as to permit them to be responsible for some part of the alpha deflections.

Alpha deflections indicate gross or total changes in the vascular bed slower than those produced by the pulse and respiratory deflections. Only a limited portion, and not necessarily all, of the vascular bed may undergo such volume changes at one time. Although the function of these shifts of blood volume is not now known, some significance seems apparent.[2]

Beta Deflections.—Beta deflections are larger waves upon which is superimposed the succession of smaller alpha deflections (Fig. 3). They vary in frequency from one-half to two per minute and their volume range is from 5 to 60 cu. mm.[2] They have been observed in all parts studied. Their frequency and volume are totally irregular, but they tend to vary concordantly in the fingers, toes and pinnae. Beta deflections are also considered to represent primarily volume changes in the vascular bed, but, as is also true of alpha

FIG. 2

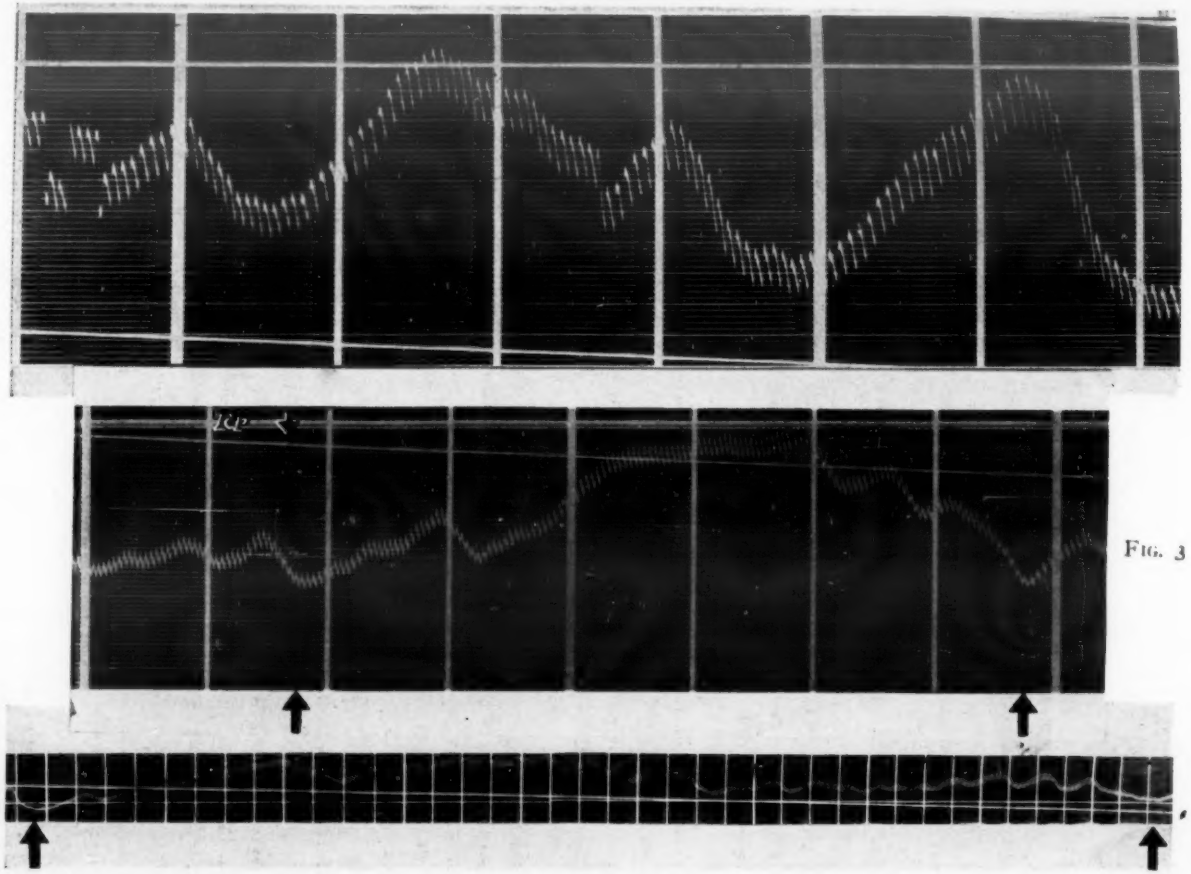

FIG. 3

FIG. 4

FIG. 2.—Plethysmogram of normal individual showing alpha deflections represented by the marked variations in the base line.

FIG. 3.—Plethysmogram of normal individual showing a positive and a negative beta deflection extending between the arrows. Alpha deflections are superimposed upon the beta deflections.

FIG. 4.—Plethysmogram of normal individual showing a positive and negative gamma deflection extending between arrows. Alpha and beta deflections are superimposed upon the gamma deflections.

deflections, a significant part of these changes may be due to variations in lymph volume. It is possible, in addition, that changes in intercellular and intracellular volume contribute to them.

Gamma Deflections.—Gamma deflections (Fig. 4) develop more slowly than any of the other deflections. They are probably concerned with large, and usually with relatively slow, shifts in blood volume from one part of the body to another. They range in frequency from one to eight per hour and in volume from 50 to 350 cu. mm.[2] Although the relationship is not necessarily constant, they show a tendency to vary concordantly in the fingers, toes and pinnae. Like the other deflections, the gamma waves are predominantly the result of changes in volume of the vascular bed of the part, with variations in lymph volume probably contributing significantly to the volume change.

NORMAL VARIATIONS IN THE PLETHYSMOGRAM

The plethysomograms of normal individuals under certain circumstances present variations of considerable degree which may resemble the changes found in diseased states. For this reason it is desirable to review them briefly. Of particular importance among the factors which may produce such changes are (1) the psychic state of the individual, (2) the environmental temperature, (3) the relation of the part to the heart level, and (4) interruption of the sympathetic pathways to the part.

Psychic State.—Both the pulse and the alpha deflections may be greatly influenced by the psychic state. Fear, anxiety, or tenseness on the part of the subject, even as a reaction to the study, tend to produce a diminution in the pulse and alpha deflections and an increase in the rate of pulse deflections,[7, 8] apparently as the result of an increased sympathetic activity associated with the psychic disturbance which causes an increase in vasomotor tone. Any change in the mental state may affect the character of the spontaneous volume deflections. Flushing or blushing, for instance, is associated with an increase in the volume of the pulse deflections and a decrease in the alpha deflections, while if the individual is comfortable and relaxed, the volume of the pulse deflections is moderate and that of the alpha deflections is relatively large.

Environmental Temperature.—The spontaneous volume deflections are considerably influenced by the environmental temperature. Chilling the subject, either by local applications or in a cool room, produces vasoconstriction and a consequent reduction in the volume of the pulse and alpha deflections. In general, the degree of vasoconstriction is proportionate to the degree of chilling. After prolonged chilling, vasodilatation may supervene, the result being an increase in the volume of the deflections, in which the alpha deflections usually exhibit a relatively greater change than the pulse deflections. With prolonged chilling, however, a negative gamma deflection also occurs, indicating a slow but definite over-all decrease in the volume of the part. As the part warms, a positive gamma deflection appears, indicating restoration of local blood volume and an over-all increase in the volume of the part.

The application of heat, either locally or in a heated room, has the reverse

effect, that is, vasodilatation occurs, with a consequent increase in the volume of the pulse deflections and a decrease in the alpha deflections, while a positive gamma deflection appears, indicating an over-all increase in the volume of the part.

It has been suggested[1] that these reactions serve as good tests for organic occlusive arterial and arteriolar disease. In such conditions as thrombo-angiitis obliterans and obliterating arteriosclerotic endarteritis the vasodilating responses are impaired or absent. The effort to produce vasodilatation in the finger tips or the tips of the toes by the application of heat to another extremity tests the patency of the arteries and peripheral blood vessels to the part under investigation, as well as its neurovascular mechanism.

Relation of Part to Heart Level.—Spontaneous volume deflections are influenced by the position of the part in relation to the heart level. A decrease in volume of the pulse and alpha deflections may be produced by placing the part below heart level, the decrease being generally proportionate to the degree of lowering of the part. The pooling of blood and lymph in the dependent part, as a result of gravity, produces a positive gamma deflection.

The exact explanation of the decrease in volume of the pulse deflection has not been definitely established, but two factors, either alone or in combination, may account for it. The first is arteriolar constriction. The second, and more likely, is distention of the vessels, with a diminution in further distensibility of the vessel walls.[9]

Elevation of the part above heart level produces results just the opposite of those produced by dependency, that is, there is a pronounced increase in the volume of the pulse deflections, and, as a consequence of the draining out of the blood within the part, a negative gamma deflection. Obviously, for standard recordings, the part should be kept at or near heart level.

Interruption of Sympathetic Pathways.—The interruption of impulses over the sympathetic pathways produces profound changes in the spontaneous volume deflections. Within a few minutes after the regional sympathetic nerves or gauglia have been blocked by infiltration with 1 per cent procaine hydrochloride solution there is a marked increase in the volume of the pulse deflections and a virtual disappearance of the alpha deflections. The latter phenomenon would be expected, since these deflections are dependent upon intact sympathetic pathways.

It has been our observation that sympathetic block produces a maximum degree of vasodilatation in the part, which cannot be exceeded, and which is seldom equaled, by any other clinical procedure. During the early phases of sympathetic block the resulting engorgement of the vascular bed within the part produces a positive gamma inscription.

Sympathetic block furnishes another significant diagnostic test.[10, 11] By this means it is easy to determine the degree of the normal, or, in certain conditions, of the abnormal, vasoconstrictor tone and the extent of vasodilatation, or the general order of the amount of increase in vascularity of the part which can be achieved by interruption of the sympathetic pathways.

THE "BORROWING-LENDING" HEMODYNAMIC PHENOMENON (HEMOMETAKINESIA)

From what has been said, it is evident that spontaneous variations are constantly taking place in the vascular bed in different parts of the body, with resulting changes in the distribution of the blood volume. These changes may occur in widely separated parts of the body. They may be rhythmic, concordant, or discordant. They may be produced by intrinsic factors not yet well understood, or they may be influenced by various internal and external stimuli. Fundamentally, they indicate a continuous shifting back and forth of blood from one part of the body to another.[12]

It has been repeatedly demonstrated that there are spontaneous variations in the volume of certain internal organs, as well as in the volume of superficial structures. Experimental studies in animals have demonstrated intermittency or irregularity in the blood flow of the renal glomeruli,[13] tongue and skeletal muscles,[14] and ear.[15] Further experimental studies on the circulation in various organs by Zweifach[16] and Chambers and Zweifach[17] have confirmed the intermittency of blood flow in various parts of the body, a phenomenon which these workers term vasomotion. The spontaneous variations in splenic volume reported by several observers[18-22] are of a magnitude and frequency comparable to those of the beta and gamma deflections observed in plethysmographic studies of human subjects.

The alpha, beta and gamma deflections observed on plethysograms clearly indicate that spontaneous shifts in the blood flow are constantly taking place within the vascular system. There is evidently a continuous "borrowing and lending" of blood (hemometakinesia) to meet variations in local requirements.

The volume of the vascular system is quite variable within certain limits. In the average normal individual (a 70-kg. man) the system is filled with approximately 5,400 cc. of blood[23] at a pressure which varies from 120 to 80 mm. of mercury, with a mean pressure of about 93 mm. Great variations can take place in the vascular bed within a relatively short period of time, especially in isolated parts of the body, but the total blood volume, under ordinary conditions, remains relatively constant.

The vascular volume of a finger or toe can be observed to double in size within a matter of minutes. The filling of this augmented vascular bed with blood, however, obviously does not imply the doubling of the total blood volume of the body, nor is there reason to believe that there exists in the body a special reservoir of blood for such purposes. Yet the blood must come from some source. The obvious explanation is that is has come from the vascular bed of other parts of the body. It is achieved without any alteration at all in the total blood volume, by adjustment of the vascular bed (Fig. 5). An increase in the volume of the vascular bed in one part of the body and a decrease by the same amount in another part increases the volume of blood in the former at the expense of the latter without any variation in the total blood volume (Fig. 5).

With disease, local needs may increase and may remain elevated for long periods of time. Should an infection develop in a finger, for instance, blood is

shifted into the finger at the expense of other parts of the body with less urgent demands, and inflammatory hyperemia results. The shift is probably brought about by the local release, as a consequence of infection, of substances which produce arteriolar, capillary and venous dilatation. In other words, the "stop-cocks" are opened locally in the finger and more blood is borrowed temporarily from other parts of the body to aid in overcoming infection.

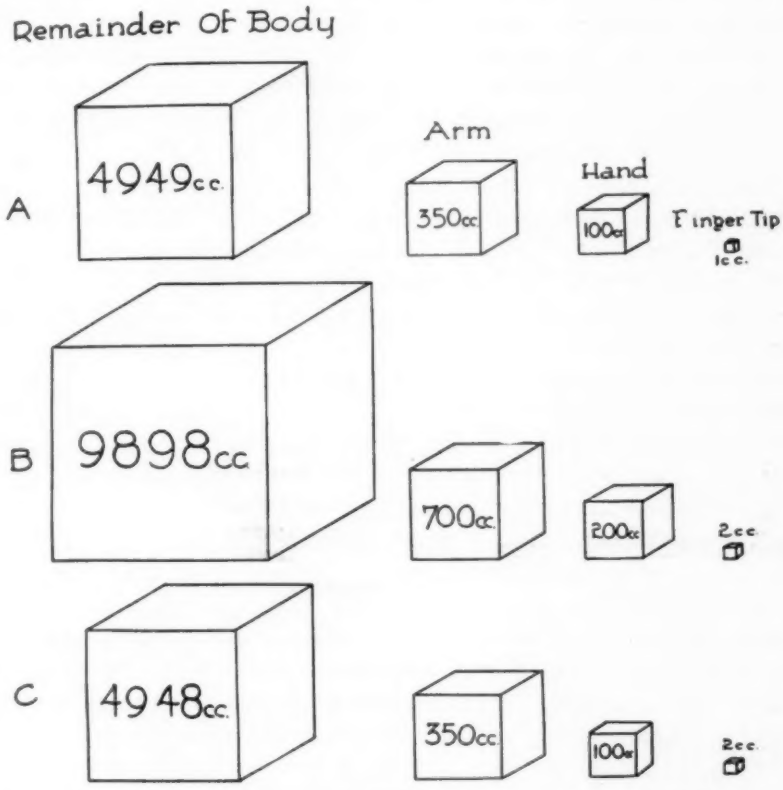

FIG. 5.—Schematic representation of the "borrowing-lending" hemodynamic phenomenon (hemometakinesia). Cubes are drawn to scale to represent volume of vascular bed in different parts of the body. A. Normal vascular bed, assuming a total blood volume of 5,400 cc. B. Vascular volume when component parts are all doubled. C. Vascular volume when blood volume of only one part, the finger tip, is doubled, with this increment of blood being derived or "lent" from the "remainder of body." It is apparent, when B and C are compared to A, the normal, that the same purpose is achieved in C as in B, the doubling of the blood volume of the finger tip, with no variation in the normal relationship in C but with obvious disturbance of it in B.

The amount of blood borrowed in this hypothetical case is relatively small, perhaps 1 cc., but it is sufficient to double, approximately, the normal local blood volume. An increase of this extent, however, in the blood supply of the finger does not disturb the general blood volume nor its hemodynamics. No effort is made by the body to double its general vascular volume in order to

double the volume in the finger. The body mechanisms do not produce for this purpose a generalized vasodilatation. This would not only be unnecessary. It would actually defeat the purpose. Were the vascular bed suddenly to double in volume, a great disproportion would develop, with equal suddenness, between the volume of the bed and the available supply of blood, and the subject, as a result, would collapse (Fig. 5).

With the total blood volume relatively fixed, it would be impossible to increase the circulating blood volume in any single part or tissue if there were a comparable increase in the volume of the entire vascular system. Furthermore, if the volume of the entire vascular bed were suddenly to double, and if the volume in one part, such as the hand, trebled, the drop in the intravascular pressure or blood pressure would be so great that the blood flow in the hand would be impaired rather than improved.

On the other hand, in the absence of generalized vasodilatation, even with maximum local vasodilatation the pressure head in the arterial system can be maintained, thus permitting in the local part an increase in volume of blood flow per unit of time. A response such as this is inevitable in order to obey fundamental principles of hemodynamics and at the same time to maintain normal circulation.

These spontaneous variations in blood volume in different parts of the body quite evidently are not mere chance occurrences. They seem, instead, to be part of a well regulated mechanism, with definite order and significance, concerned with certain vital functions such as proper thermal regulation, nutrition, repair, hemodynamics and other physiologic adjustments.

It is conceivable that at least a part of this significance lies in the attempt by the body to utilize its total blood volume in the most efficient possible manner. Obviously, the total blood volume in the body at any one time is too small to meet the maximum demand of all the tissues at the same time should a disease state arise to precipitate such a situation. On the other hand, it is more than sufficient to meet urgent local demands for large quantities of blood in isolated parts such as a finger, hand, foot, or even an entire extremity.

SPECIAL STUDIES

Numerous observations made upon normal individuals as well as on patients with various forms of peripheral vascular disease have invariably been consistent, regardless of the methods employed to determine and record variation in blood flow. Special studies have been made by thermometric and plethysographic methods.

These studies are done routinely, under controlled atmospheric conditions, in a room constructed to reduce psychic disturbances. Following rest in bed for a sufficient period of time to permit stabilization of the vascular system plethysmograms are obtained for the distal phalanges of the fingers and toes (usually the index finger and the second toe) as well as of the pinnae. Thermograms are obtained for these parts as well as for other areas; a total of 20 areas, distributed bilaterally and symmetrically, is usually observed. Plethys-

mographic and thermometric observations are usually made simultaneously. The response to such measures as interruption of sympathetic innervation, reactive hyperemia, drugs, environmental and local temperature changes, and psychic and neurogenic factors are observed as reflections in the plethysmograms and thermograms.

Observations made upon two patients, selected from the large number upon whom these studies were made, are presented to illustrate the "borrowing-lending" phenomenon (hemometakinesia):

First Patient.—G. Y., a white male 45 years of age, suffered with mild intermittent claudication due to early senile arteriosclerosis. Plethysmographic and thermometric studies were made after the patient had rested in bed in the observation room (room temperature 78° F., relative humidity 70 per cent) for 60 minutes. The skin temperature determinations were made bilaterally for the third toe, the dorsum of the foot, the mid pretibial area, the knee, the mid thigh, and the chest. The plethysmographic determinations were made for the distal phalanges of the right index finger and for the second toe on each side. After a state of stabilization had been reached, a left lumbar sympathetic block (first through fourth ganglia) was performed with 1 per cent procaine hydrochloride solution.

Within a few minutes after the performance of left lumbar sympathetic block the following events occurred simultaneously (Fig. 6):

1. A rapid elevation of the skin temperature of the left leg, with marked flushing.
2. A significant increase in the volume of pulse deflections of the left second toe.
3. An increase in the total volume of the tip of the left second toe.
4. A fall in the skin temperature of the right leg and the chest.
5. A decrease in the volume of the pulse deflections of the right second toe and right index finger.
6. A decrease in the total volume of the tip of the right second toe.

These changes indicated a marked vasodilatation in the left lower extremity after sympathetic block, with a considerable increase in the volume of blood and rate of blood flow. Blood was "borrowed" by the left leg at the expense of the remainder of the body. It was "lent" by the right leg and right index finger, as indicated by the cooling of the skin and the decrease in volume of pulse deflections and the total volume of these parts.

The expense of the shift, however, was not borne entirely by the right leg and right hand, since the vascular changes indicating a decrease in blood volume and blood flow were not as great as those reflecting the increase in the left leg. This might be expected. When relatively large quantities of blood are shifted to a part as large as the lower extremity, no single part of the body would be expected to suffer the entire loss, even if it were capable of "lending" it all. An index finger obviously would not be able to meet the whole demand, even if all its blood were shifted to the leg. Furthermore, if all the blood of a part such as the finger were shifted to the area of special need, the lending part would suffer serious damage from ischemia. Normal physiologic adjustments provide a mechanism whereby no organ is made to give up or "lend" its blood to an extent which would produce serious injury. Depending upon the quality and quantity of the shift, every organ that can afford to "lend" blood elsewhere does so. Under ordinary circumstances, however, each organ gives up only a small fraction of blood, and the changes reflecting a decrease in blood supply are relatively small in any one part under observation.

Second Patient.—J. H., a Negro male 34 years of age, who was suffering with a marked anxiety neurosis, was subjected to the same tests as the first patient and was also studied by certain additional procedures. A venipuncture was performed initially, with much deliberate manipulation, in order to produce pain and anxiety and to induce psychic

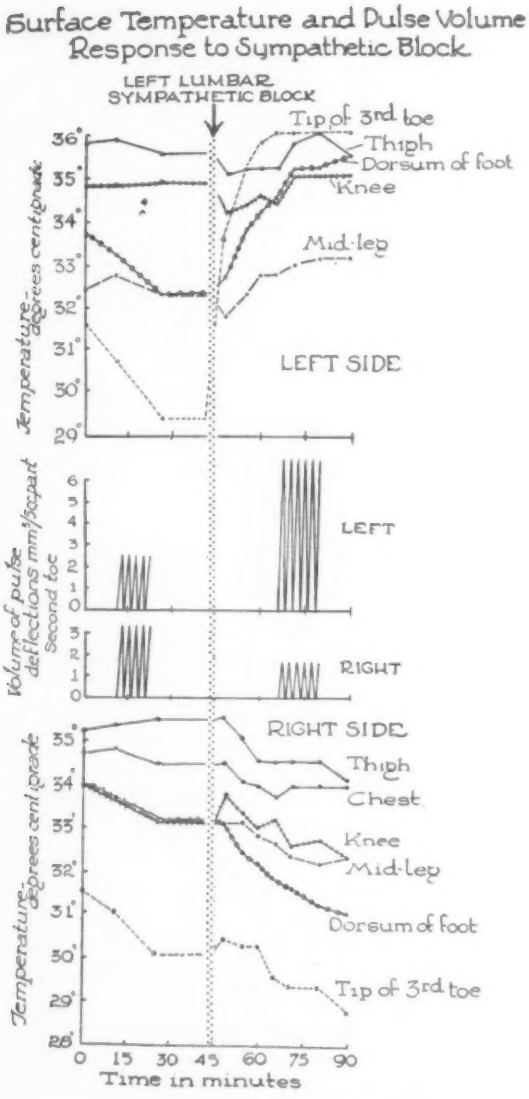

FIG. 6.—Surface temperature and pulse volume responses to left lumbar sympathetic block. It is obvious from the chart that following the block there was vasodilatation with increased blood flow in the left lower extremity, indicating the "borrowing," while on the right side there is evidence of diminished blood flow, indicating "lending" of blood.

tension and consequent diffuse vasoconstriction. After the vascular state had been stabilized at the level of vasoconstriction, 5 cc. (500 mg.) of tetraethylammonium chloride was injected intravenously. Then, after sufficient time had elapsed for the reaction to subside, a left posterior tibial nerve block was performed, using 1 per cent procaine hydrochloride solution. Two and a half hours later, a left lumbar sympathetic nerve block (first through fourth ganglia) was performed, using the same drug.

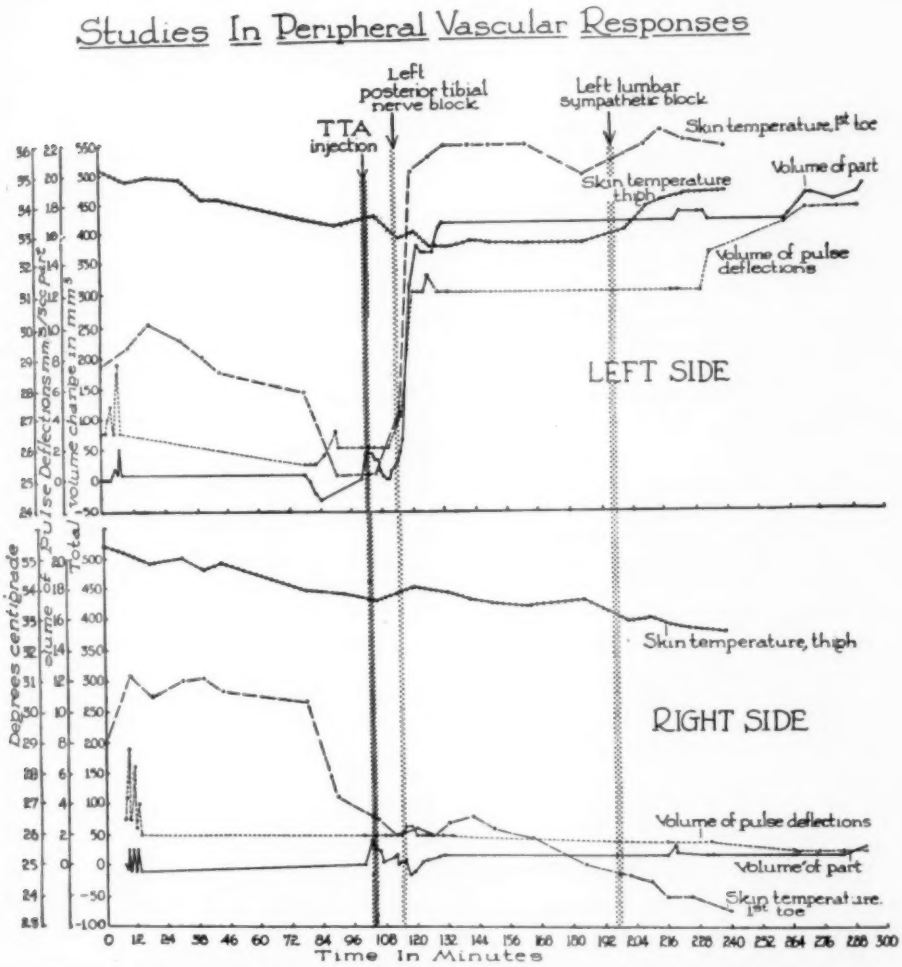

FIG. 7.—Graph showing thermometric and plethysmographic changes following injection of tetraethylammonium chloride (T. T. A.), left posterior tibial block and left lumbar sympathetic block.

The phenomena observed in the first patient are still further clarified by the results obtained in the second patient (Fig. 7):

The anxiety following the traumatic venipuncture resulted in considerable decreases in skin temperature, in the volume of pulse deflections, and in the total volume of the tips of the finger and toes studied. All these findings are evidence of diffuse vasoconstriction.

After the administration of tetraethylammonium chloride, which has been reported to produce vasodilatation,[24] there was little or no change in the skin temperature or in the

volume of the tips of the second toes, and only a slight increase in the volume of the pulse deflections of the finger and toes studied. Very little vasodilatation was to be expected. With generalized vasodilatation, each organ must "lend" and "borrow" at the same time, which is impossible unless the blood volume or cardiac output or both are increased to meet the demands occasioned by diffuse dilatation. Any drug which is a strong vasodilator would be expected at least to restore the state of the blood vessels of the superficial portions of the body to resting normal levels, which tetraethylammonium chloride did not do in this case. Furthermore, there is no evidence to show, nor any reason to expect, the sympatheticolytic effects to be greatest where the sympathetic tone is greatest. If the drug acts equally throughout the sympathetic ganglia, diffuse vasodilatation would be expected to result in little change in the blood supply to a particular part unless blood volume or cardiac output or both were increased.

Following left posterior nerve block the following changes were observed (Fig. 7):

1. An increase in the skin temperature of the left first toe.
2. An increase in the volume of pulse deflections of the second toe.
3. An increase in the total volume of the tip of the left second toe.

There were no changes on the right. The changes on the left, it should be noted, occurred in spite of the patient's state of anxiety and after the administration of tetraethylammonium bromide had failed to produce vasodilatation. Since the amount of blood that would be borrowed by a part as small as a foot to meet even maximum vasodilatation is relatively small, no measurable evidence of "lending" would be expected to be observed in other portions of the body, especially since each part might participate in supplying only a very small amount of blood.

At the end of two and a half hours there was relatively little change in the state of the circulation under observation. When left lumbar sympathetic block was done at this time, the following changes occurred:

1. A further increase in the temperature of the skin of the left leg and thigh.
2. A further increase in the volume of pulse deflections of the left second toe.
3. A further increase in the total volume of the tip of the left second toe.
4. A slight decrease in the volume of pulse deflections of the right second toe.
5. A slight but definite decrease in the temperature of the areas with intact sympathetic innervation.

After left lumbar sympathetic block, the volume of blood shifted to the whole left leg was evidently much greater than that following tibial nerve block, and, as in the first patient, evidence of a shift of blood from the right leg and right hand were obtained (Figs. 6 and 7).

DISCUSSION

The evidence now at hand seems to justify the following statements:

1. There is a continuous shifting back and forth of blood from one part of the body to another.

2. The "borrowing" and "lending" of blood (*hemometakinesia*) from tissue to tissue to meet variations in local requirements seem indicative of a well regulated mechanism which permits the body to utilize its limited total blood volume in the most efficient manner.

3. The essence of this mechanism seems to lie in the control and regulation of the vascular bed, which permits an increase in the volume of blood of one part of the body with a corresponding simultaneous decrease in the volume of blood in other parts.

4. The variation of the blood volume in different parts of the body does not involve any alteration in the total blood volume.

5. Variations in cardiac output, however, can produce changes in blood flow to a part independent of changes in blood volume.

The application of these principles of hemodynamics to peripheral vascular disease immediately suggests itself: Peripheral vascular disease is characterized by a disturbance of, or actual diminution in, the normal amount of circulating blood which reaches the part, and its effective therapy is based on improvement in the circulation or an increase in the blood supply of the part. Therapeutic measures designed to produce dilatation of the entire vascular bed do not seem rational for a disease state localized to a single peripheral part, but, in spite of the illogic of the attempt, there are numerous reports concerning the production of generalized vasodilatation as a form of therapy for peripheral vascular disease involving portions of the body. The results of these efforts are open to question; theoretically such measures are inefficient. Moreover, even if an effective agent, *i.e.*., with the ability to produce *maximum* vasodilatation, for this purpose did exist, its effects would be dangerous; the reaction would be shock-like, and the original purpose of increasing the blood supply to the local part would be completely defeated.

In view of the lack of rationale in peripheral vascular disease of the use of agents intended to produce generalized vasodilatation, quite aside from their ineffectiveness and theoretical dangers, the attention should be concentrated on measures which produce local vasodilatation. The best of these measures, in our experience, is sympathetic denervation of the affected part. It is rational, because it conforms with the principles of hemodynamics just laid down; it produces local vasodilatation insuring maximum improvement in the local circulation of the diseased part. It is safe, because it does not reduce the arterial blood pressure or produce serious systemic disturbances by the sudden creation of a disproportion between the total volume of the vascular bed and the total blood volume. Finally, it is effective. Theoretically, when this procedure is used, there should be a definite and significant increase in blood supply to the diseased part. Practically, there is such an increase, as is demonstrated by the two cases presented in this communication, which were selected from a large experience.

Indeed, we have yet to find a general vasodilator which could produce in a local part, such as the toes, fingers, foot, hand, or extremity, vasodilatation equal in degree or duration to that produced by sympathetic denervation of the part.

SUMMARY

1. Although gaps still exist in our knowledge of the hemodynamics of the peripheral circulation under normal resting conditions and in disease states, the evidence at hand justifies certain statements:

A. That there is a continuous shifting back and forth of blood from one part of the body to another; for this "borrowing-lending" mechanism the term *hemometakinesia* is proposed. B. That hemometakinesia seems to indicate the existence of a well regulated mechanism which permits the body to utilize its limited total blood volume in the most efficient manner to meet variations in

local requirements. C. That the essence of this mechanism seems to lie in the control and regulation of the vascular bed, which permits an increase in the volume of blood of one part of the body with a corresponding simultaneous decrease in the volume of blood in another part without any alteration in the total blood volume.

2. It is suggested that these principles of hemodynamics are applicable to the management of peripheral vascular disease, the effective therapy of which is based on improvement in the circulation or an increase in the blood supply of the part. Measures directed toward the improvement of the local circulation by production of dilatation of the entire vascular bed are of doubtful value, whereas measures directed toward local vasodilatation are in conformity with the natural "borrowing-lending" mechanism (hemometakinesia).

3. The most effective method of increasing the local blood supply is sympathetic denervation of the affected part. In addition, it is in complete conformity with the concept of hemometakinesia.

4. Two cases, selected from a large experience, are presented to illustrate the concept of hemometakinesia and to demonstrate the value of sympathetic denervation as a therapeutic measure in peripheral vascular disease.

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ARTERIAL INJURIES*

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Wounds of major arteries in World War II proved unexpectedly serious as regards survival of the affected limb. The experience of the past seemed to indicate that ligation of torn vessels in the course of debridement was in most instances the practicable method of handling these cases although suture repair and tube anastomoses had been reported. The large number of amputations for ischemic extremities brought about efforts to suture arteries and to bridge gaps by tubes, or venous grafts after the method of Blakemore and Lord.[1] While the value of these methods from the reports so far available, as well as from the series to be presented, cannot be proved statistically, the outcome in individual cases is sufficiently encouraging to warrant further trial in civilian practice.

The basis for this study consists of 114 wounds of major arteries seen in an Evacuation Hospital in the European Theater of Operations together with four primary cases operated on in a General Hospital in the same theater. For purposes of comparison with other reports the Evacuation Hospital cases are tabulated separately. The General Hospital cases were not battle casualties. They are presented after the others and included with them in the discussion.

MORTALITY

Patients succumbing before, during or immediately after operation have been omitted since the purpose of the study is the incidence of gangrene and measures to lessen it. There were four such fatalities from hemorrhage and shock during the evacuation hospital period. These included one wound of the iliac, two of the femoral and one of the popliteal.

Among the cases included in the series there were four deaths. Two of these had come to amputation for gas gangrene, one died with anuria, and the fourth, a civilian woman, died suddenly the day after operation. She had an amputation of the leg in addition to a wound of the brachial artery which was progressing quite satisfactorily. In general, if a patient with a major vascular wound reaches a hospital his chances of life, if not of limb, are pretty good.

Results of injuries to the major vessels of the extremities appear in Table I.

An attempt was made to keep patients with extremities of doubtful viability until the issue was clear. It was at times impossible, however, so that there may be some error in estimates although it is thought to be small. Necrosis of fingers or toes sufficed to record the outcome as gangrene.

Reports from other Evacuation Hospitals [2, 3, 4] in the ETO substantiate the serious outlook for major arterial wounds as indicated in Table I. On

* Read before the American Surgical Association, March 25, 26 and 27, Hot Springs, Virginia.

the other hand the much more favorable experience which some of the World War I figures show are due to inclusion of cases of arteriovenous and traumatic aneurysms picked up in rear echelons. Few of these in my experience were apparent at the evacuation hospital stage.

TABLE I

EVACUATION HOSPITAL CASES

Vessel	Number of Cases	Gangrene	% Gangrene
Axillary	5	2	40
Brachial	51	18	35
Femoral	25	20	80
Popliteal	21	15	71
Post. tibial* (upper end)	7	4	57
Ant. and post. tibials	5	2	40
Total	114	61	54%

* Wounds of the posterior tibial in the lower part of the leg are not of themselves particularly dangerous and are not tabulated.

TREATMENT

It is obvious that a lateral tear only of the artery represents the condition most favorable for suture. When a segment of the vessel is carried away so that a graft or tube is necessary to bridge the gap the outlook is much worse. Last but not least the extent of damage to the surrounding tissues in which collateral circulation can carry on has probably been the most important factor in the loss of many limbs.

Table II summarizes the experience of attempts at arterial repair in the Evacuation Hospital series.

TABLE II

ARTERIAL REPAIR EVACUATION HOSPITAL CASES

Vessel	Suture	Gang.	Suture Anast.	Gang.	Tube Anast.	Gang.	Vein Graft	Gang.	Total	Gang.	% Gang.
Brachial	2	0	1	0			1	1	4	1	25
Femoral	2[a]	1	1	1	1[b]	1	1	1	5	4	80
Popliteal	1	0			2	1			3	1	33
Post. tibial	1	0			1	1			2	1	50
									14	7	50

[a] Both sutures of incision after removal thrombus.
[b] Attempted after two days.

SUMMARY OF EVACUATION HOSPITAL CASES

Brachial Artery (4 cases).—The brachial artery of an American soldier was torn half way across in the upper third. The extremity was warm but pulseless. Following suture of the vessel there was a good recovery.

An American soldier received multiple wounds, in one of which the lower brachial was divided except for a thin bridge of intima remaining posteriorly. There was no pulse and no oscillometric reading in the extremity although it was fairly warm. The vessel was sutured about 15 hours after injury. A day after operation the radial pulse and small swings of the oscillometric needle were noted.

A German civilian woman suffered multiple mine wounds including division of the brachial in the lower third. The vessel was sutured 24 hours after injury. The next day the pulse was faintly perceptible and on oscillometric examination there were flickers of the needle. The patient died suddenly, 36 hours after injury. Postmortem examination of the anastomosis showed a soft non-adherent clot extending one centimeter upward and two down.

An American soldier received a severe wound of the arm, dividing the brachial artery and the median nerve in the upper third and fracturing the humerus. The extremity was cold and pulseless. Six hours after injury the gap in the artery was bridged by a vein graft using vitallium cuffs. The hand never became warm, nor was any pulse perceptible. At the time of evacuation six days after operation the fingers and thumb were black.

Femoral Artery (5 cases). The femoral artery of an American soldier was divided in Hunter's Canal. The foot was cold. The gap between the vessel ends was bridged by a vein graft with vitallium cuffs. No distal pulse was obtained subsequently. At transfer on the 12th day it appeared that at least part of the foot would be lost.

A German boy of eight was brought in with a wound in which the distal end of the femoral artery had been divided. End-to-end suture was done. It appeared that he would eventually come to amputation when he was evacuated on the 5th day.

An American soldier was admitted with an extensive wound of the upper thigh in which the superficial femoral artery was found to be thrombosed shortly below the profunda branch. As the foot was warm it was hoped that the circulation would remain adequate. In the course of the next 48 hours the foot became cold and an attempt was made to save the situation by a tube anastomosis. In view of the time elapsed this was ill-advised. There was no benefit and amputation became necessary.

Two American soldiers with thrombosis of the superficial femoral were treated by incision of the artery, removal of the thrombus and suture. In one of these men a faint pulse was felt distally 45 minutes after operation and thereafter could be obtained on careful examination. The other man had in addition to his femoral thrombosis a fracture of the femur. When discharged on the 7th day he had gangrene of the first and second toes.

Popliteal Artery (3 cases). An American soldier was admitted with a gaping wound of the popliteal space. The femur was fractured and the artery divided with ends far apart. The opposite femur also was fractured. The gap in the popliteal artery was bridged by a plastic tube 24 hours after injury. The veins of the foot were observed to fill and color appeared in the skin. Twenty hours after operation the foot was warm but eight hours later had become cold again and went on to gangrene. The patient died on the 5th day with a progressive oliguria. At autopsy the tube contained a soft clot which extended 4 to 5 cm. into the artery above and below.

An American soldier suffered division of the popliteal artery by a small shell fragment which did little other damage. The foot was cool rather than cold, pulseless, and the leg without oscillometric response. Eleven hours after injury a plastic tube anastomosis was done. The pulse could be felt immediately after operation and good oscillometric swings obtained. These continued until the 7th day when, without change in warmth of the foot, the distal pulse could no longer be felt nor could an oscillometric reading be made. On the 13th day the pulse could again be faintly felt. The next day the tube was removed. It was filled with clot. The dorsalis pedis continued to be faintly palpable and the patient was evacuated with an intact extremity.

An American soldier's popliteal artery was torn about three-fourths through its circumference in the lower part of its course. The laceration was sutured. Postoperatively

there was some pain and swelling in the leg but when the patient was evacuated on the 6th day he could move the toes, and the foot was warm.

Posterior Tibial Artery (2 cases). An American soldier had his posterior tibial artery divided above the peroneal branch and both bones of the leg fractured by shell fire. The extremity was cold. A plastic tube anastomosis was done with no immediate nor late improvement and amputation had to be carried out four days later.

A German girl of 16 was brought in with a shell wound of the leg which fractured both bones, divided the anterior tibial artery and made a lateral wound in the posterior tibial in the lower third of the leg. The pulses were absent in the foot which was dusky and cool. At operation 10 hours after injury the posterior tibial was sutured. Recovery was slow but by the 5th day the foot was warm and the circulation was thought to be adequate.

In Table III the result of arterial repair as compared with ligation and series as a whole is presented together with like data from other Evacuation Hospitals.

TABLE III

	Suture		Non-Suture Anast.		Combined			Ligation			Whole Series		
	No.	Gang.	No.	Gang.	No.	Gang.	% Gang.	No.	Gang.	% Gang.	No.	Gang.	% Gang.
This study	8[a]	2	6	5	14	7	50	58[b]	32	55	114[c]	61	54
Rose, Hess & Welch	5	0	8	6	13	6	46	70	37	53	91[d]	45	49
Bradford & Moore	6[e]	1	5	3	11	4	36	87	39	45	110	46	42
Stewart	0	0	5[f]	2	5	2	40	33	17	52	38	19	50
Totals	19	3	24	16	43	19	44	248	125	50	353	171	48

[a] Includes two cases thrombectomy.

[b] A number of cases are omitted because the record does not specify as to ligation.

[c] The discrepancy between the sum of those treated by operation and by ligation, 72, and the whole series, 114, is made up of those in whom nothing was done to the vessel and in whom the records are not sufficiently clear to classify, although it is probable that most of this group were ligated.

[d] Cases of primary amputation omitted.

[e] Includes one case thrombectomy.

[f] Dr. Stewart reported two additional cases in which non-suture anastomosis was attempted but they are omitted from the table because they occurred at a period previous to that from which the rest of his series was compiled.

In Table IV figures from the much larger series of Odom[5] and DeBakey and Simeone[6] are presented for comparison with these of Table III. Doctor Odom was surgical consultant to one of the European Armies while the figures of Doctors DeBakey and Simeone were compiled from the records available in the Surgeon General's Office.

TABLE IV

	Suture		Non-Suture Anast.		Combined			Ligation			Whole Series		
	No.	Gang.	No.	Gang.	No.	Gang.	% Gang.	No.	Gang.	% Gang.	No.	Gang.	% Gang.
Odom	42	23	28	14	70	37	53	767	386	50	857	423	51
DeBakey & Simeone	81	29	54	30	135	59	44	1639	802	49	2471	995	40

SUMMARY OF GENERAL HOSPITAL CASES

A German prisoner was wounded by a small fragment of cartridge which exploded in a bonfire. It divided the brachial artery 1 to 2 cm. above its bifurcation in the forearm. The radial pulse was absent and the extremity cooler than its fellow. The artery was sutured. Immediately after operation the pulse could not be felt but on examining him seven hours later it was just palpable. It became strong before transfer.

A German prisoner slipped, thrusting his elbow through a pane of glass. The brachial artery and median nerve were divided below the middle of the arm. At operation three hours after injury the ends of the artery could be approximated with slight tension and were sutured together. The lower end of the median nerve was not found at this time. Immediately after the operation a radial pulse could not be felt but within an hour it was faintly palpable. On the 16th postoperative day the median nerve was sutured. At this operation although pulsation was present just below, it could not be felt at the site of anastomosis.

A Polish soldier was accidentally shot through the lower thigh with a pistol. The lower end of the femoral artery was divided except for shreds and the vein torn. An end-to-end anastomosis of the artery was made with some difficulty as the knee had to be flexed to approximate the torn ends. The vein was ligated and the leg put up in plaster to maintain flexion. The foot warmed up within a few hours after operation but distal pulses had not been felt at the time he left the hospital one month later.

The popliteal artery of an American soldier was completely torn through opposite the joint in a truck accident, apparently as the result of hyperextension of the knee. There was considerable hemorrhage into the popliteal space. The vein and nerve were intact. As approximation of the torn ends was impossible, a plastic tube anastomosis was done. The lower end of the vessel was found with difficulty and would only take a small tube. No immediate effect was noticeable but 12 hours later the foot, which had been cold, was warm. It soon became cold again and amputation through the thigh was eventually necessary.

DISCUSSION

Suture. Including both Evacuation and General Hospital cases, but excluding the two in which suture was of the thrombectomy incision, there were nine arterial sutures with one subsequent gangrene. This would seem to indicate that suture is quite successful as compared with other methods. It must be remembered, however, that it is possible only in lateral wounds or those with limited separation of the divided ends, and therefore, in general, in the less severe injuries. Furthermore the majority of sutures here reported were done in wounds of the brachial artery, in which the outlook for survival of the arm was favorable.

That clotting is likely to take place at the suture site raises the question as to whether the extra time consumed as compared with simple ligation is justified. The ideal, of course, is that the channel remain open, but there is reason to hope that even though clotting occurs, enough blood will get through to maintain viability until the collateral circulation can take over.

The Medical Research Council (Britsh)[7] states: "As a general rule it takes four days in the arm and 14 days or more in the leg for the distal pulse to return after ligature of the main artery." Individual cases vary. Rose, Hess and Welch have noted palpable radial pulsations 24 to 72 hours after ligature

of the brachial artery. In a patient in this series whose brachial had to be ligated at the lower end radial pulsations were questionable at the end of 48 hours and present in 72 hours.

In two patients with sutured brachials a radial pulse was noted after 24 hours. In one of the general hospital cases with a suture anastomosis at the lower end of the brachial the pulse was felt seven hours after operation. It had not been examined in the interval since leaving the operating room.

As a result of this experience the next patient was observed more closely. After suture of his brachial in the lower half of the arm the radial pulse could not be felt in the operating room but within an hour after return to the ward it was just palpable. It seems probable that blood carried through the site of anastomosis contributed to this finding.

Plastic tube anastomosis. There were five cases with gangrene in four. One of the plastic tube anastomoses of the popliteal in this series resulted most satisfactorily, postoperative observations seeming to indicate that blood was carried through it for six days, at which time collateral circulation was adequate. This patient's wound, however, was relatively small, and the foot never more than cool so it may well have been that his collateral circulation was sufficient from the beginning. In two other tube anastomoses of the popliteal there was encouragement from the warming of the foot only to see it become cold again after 24 hours and go on to gangrene.

Venous graft. There were two cases with gangrene in both. It is more difficult technically than tube anastomosis and failure in these cases may have been due to lack of experience with the method.

Heparin. In debrided battle wounds the employment of heparin parenterally involves a risk. In the arterial injuries of civilian life, however, it is to be hoped that it may be employed, as experience both experimental and clinical has shown its value. It was used locally in some instances in this series but was unavailable in amount sufficient for systemic heparinization.

Thrombosis. If a vessel is contused by a missile, thrombosis may result. DeBakey and Simeone reported 70 per cent amputation following 44 cases of thrombosis. In this series there were ten cases recorded of whom four developed gangrene. In two of these, both of the femoral in its midposition, the artery was incised, the clot removed and the vascular wound sutured. One kept a viable foot and the other developed gangrene of the first and second toes.

Sympathetic Block. Sympathetic block was tried in a large number of the cases in this series with disappointing results. The disappointment probably is to be attributed to the hope that it would benefit cadaver-like limbs in which not only the main blood channel but much of the collateral circulatory bed was damaged. It seems reasonable to expect that in cases where the margin between a sufficient and an insufficient blood supply is narrow, it may serve to turn the scale.

Ligation of accompanying vein. This subject is raised as the question has excited so much interest. In this series there is insufficient data to draw any conclusion.

SUMMARY

Battle wounds involving the femoral and popliteal arteries have resulted in subsequent gangrene in a large proportion of cases. Those of the brachial were followed by loss of the extremity in over a quarter.

Suture of lateral wounds of the arteries should ordinarily be done, and end-to-end sutures in cases where it is practicable.

The use of glass and plastic tubes, or venous grafts to bridge gaps does not seem, from the statistics available, to have improved results, yet a consideration of individual cases justifies further trial.

In the surgery of civilian vascular injuries, particularly those in which large debrided areas do not have to be left open, heparin offers an opportunity of bettering the outcome.

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SYMPATHECTOMY FOR OBLITERATIVE ARTERIAL DISEASE; INDICATIONS AND CONTRAINDICATIONS*

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THE PURPOSE OF SYMPATHECTOMY in the treatment of peripheral vascular disease is manifestly to abolish the vasomotor tone in order to improve the circulation and to allow development of collateral blood vessels. The greater the impairment of circulation by vasoconstriction, the better are the results to be expected from sympathetic denervation. In those cases, however, in which vasomotor tone is low, sympathectomy may be of little value. In addition, widespread sympathectomy, may actually produce harm by lowering the peripheral resistance, especially in cases where there is severe arterial obliteration. This paper presents an evaluation of sympathectomy in the treatment of obliterative arterial disease, and a discussion of the indications and contraindications for the use of this form of treatment.

The peripheral circulation serves a dual function. By means of blood flow through the capillaries the nutrient demands of the tissues are met. In addition, the peripheral circulation to the extremities in man serves the purpose of regulating the body temperature. In accordance with the requirements for conservation or dispersal of heat, the circulation to the extremities is reduced or expanded. This dual function of the circulation is mediated by a dual control. With vasomotor nerves intact, the circulation through the distal parts of the extremities can be shown to be influenced reflexly through stimulation or inhibition of the sympathetic nerves. After removal of this vasomotor control by sympathectomy the circulation is dependent upon the metabolic requirements of the tissues.[1]

In view of this dual function and dual control, the presence of a dual anatomic structure is to be expected. That such is the case was shown originally by the researches of Sucquet[2] and Hoyer.[3] They first described the neuromyo-arterial glomus, a vascular arrangement quite distinct from the nutrient capillaries, which, in man, was found chiefly in the distal parts of the extremities. The studies of E. R. Clark[4] on the rabbit ear provided knowledge of the structure and activities of these arteriovenous anastomoses in the experimental animal. Understanding of the physiology of these structures was made possible through the investigations of Grant[5] and Bland.[6] By means of these communications between the terminal arteries and the small veins of the extremities, blood can rapidly be shunted from the arterial to the venous system

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without passing through the capillary network. Grant[5] showed that these communications were under vasomotor control since stimulation of the sympathetic nerves caused them to close, as did the injection of adrenalin. Clark[4] observed that injury to the nerve caused the arterio-venous anastomosis to remain continuously dilated for 10 to 14 days. After that time, the smooth muscle apparently acquired tonicity and the lumen thereafter was maintained at a narrow calibre. This observation may help to explain the evanescence of cutaneous vasodilatation after nerve injury, although it fails to account for the persistent

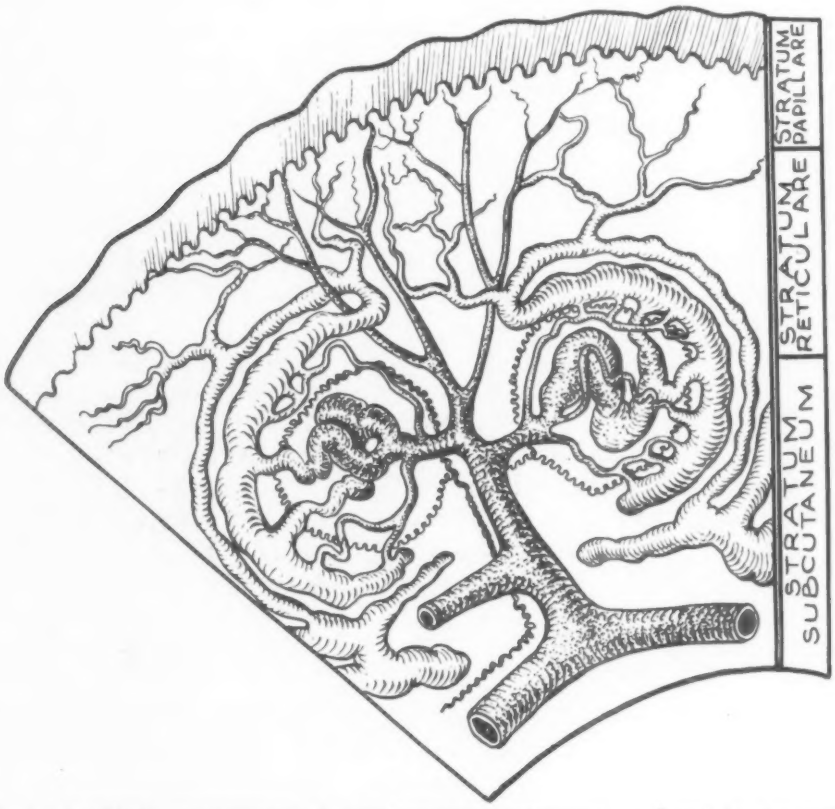

FIG. 1.—Anatomic arrangement of arteriovenous anastomoses as found in the ventral surface of the digit. (Redrawn after Popoff. Arch. Path. 1934.)

and prolonged vasodilatation, especially in the lower extremities, which follows sympathectomy. From observations on experimental animals and man, it seems likely that the increased peripheral skin temperature which follows interruption of sympathetic impulses is mainly due to opening up of these arterio-venous communications.

Popoff[7] called attention to the significance of these arterio-venous anastomoses in peripheral vascular diseases after careful anatomic studies with reconstruction from serial sections. The anatomic arrangements are shown in Figure

1, which has been redrawn from Popoff's paper. He stressed the fact that when arterial blood passes directly into the veins without going through the capillary network, serious deprivation of the tissues may result. In addition, in thrombo-angiitis obliterans he described abnormal arterio-venous communications which might lead to a rapid dumping of the arterial blood into the veins. Figure 2 represents a schematic drawing of the A-V anastomoses taken from Popoff's original work. Microscopic changes in the veins led him to conclude that "Arterialization of the veins is evidently the result of adaptation of the veins to abnormal strain created by an uncontrollable flow of blood through the artero-venous anastomosis." In one patient he even went so far as to compare the oxygen saturation of blood obtained from a vein on the dorsum of the

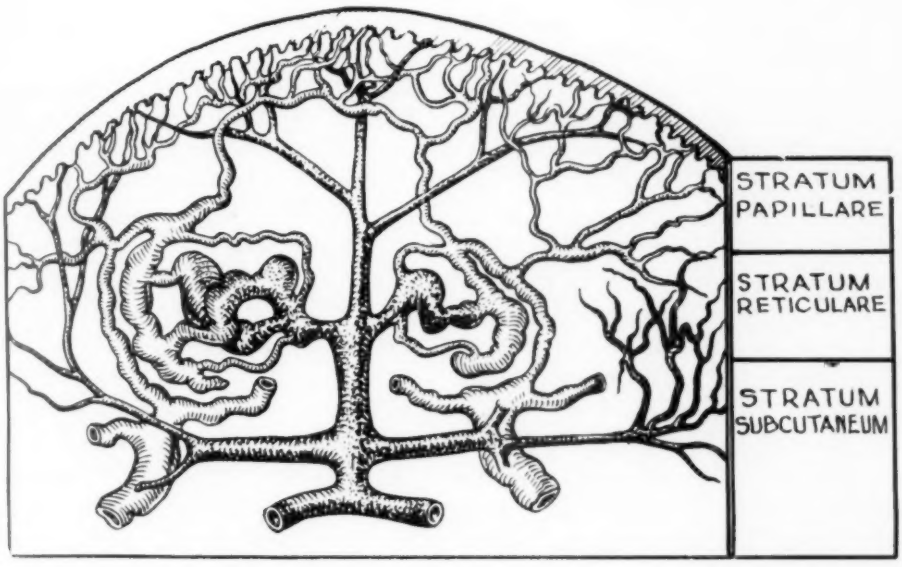

FIG. 2.—Diagram demonstrating two types of anomalous arteriovenous anastomoses found in thromboangiitis obliterans: the lateral type and the terminal type of anastomoses. (Redrawn after Popoff. Arch. Path. 1934.)

foot with that of blood simultaneously obtained from a forearm vein. As he expected in view of his anatomic studies, he found that the oxygen saturation of the blood from the veins of the foot was considerably higher than that of the blood obtained from the arm, suggesting that the blood in its passage from the arteries to the veins had not traversed the capillary loop. This observation was confirmed and extended by Harpuder, Stein, and Byer,[8] in a series of cases. Some of the highest oxygen values which they found were in cases in which the disease was the most advanced. They concluded that "shunt circulation, for practical purposes, is a loss as far as tissue metabolism is concerned." To Atlas[9] goes the credit for having suggested that the disastrous results occasionally encountered after sympathectomy in advanced arterial obliterative

disease were due to opening up of these small arterio-venous communications.

The chief indication for sympathectomy is abnormal vasoconstriction or vasospasm. In extreme cases such as the digital syncope of Raynaud's phenomenon, the diagnosis of this condition is simple, but it is far more difficult to arrive at a sound basis for making this diagnosis in the less severe cases.

Brown[10] was the first to approach the problem of placing vasomotor tone in man on a quantitative basis. He compared the rise in skin temperature of the digits with the rise in mouth temperature after the administration of typhoid vaccine. The change in the surface temperature of the digits gave an index of vasodilatation. Morton and Scott[11] used anesthesia, general, spinal or local, to abolish vasomotor tone. They designated the average maximum vasodilator response of undiseased arteries as "the normal vasodilatation level." White[12] was the first to use paravertebral injection of procaine to block the sympathetic nerves to the extremities as a test to evaluate the potential benefit of sympathetic ganglionectomy. The vasodilatation with rise in skin temperature which occurs upon heating the unaffected extremities or portions of the body was employed by Gibbon and Landis[13] to differentiate vasospastic from occlusive arterial disease. All of these vasodilatation tests are useful in estimating the degree of organic vascular occlusion, but they do not indicate the relative degree of vasoconstriction which is intermittently or constantly affecting the blood supply to the peripheral tissues. Vasoconstriction is the normal physiologic response of the body to cooling. It occurs both in normal patients and in those with diseased or injured blood vessels. The vasodilatation tests indicate only to what extent the peripheral blood vessels can dilate; they do not measure the degree of vasoconstriction.

In order to make the diagnosis of abnormal vasoconstriction, certain clinical signs have been utilized. In the selection of patients with intermittent claudication for sympathectomy, the combination of peripheral cyanosis, increased sweating, and constriction of superficial veins of the extremities was used by Freeman and Montgomery[14] as clinical evidence of high vasomotor tone. Experience with sympathectomy in obliterative arterial disease during the past five years leads us to re-emphasize the significance of these clinical signs of abnormal vasoconstriction. Possibly less attention is paid now than formerly to the prominence of the veins on the dorsum of the foot, since we have repeatedly observed patients whose veins were prominent, but in whom other signs indicated a high degree of vasomotor tone. Constricted veins, however, are still looked upon as good evidence of abnormal vasoconstriction. One further observation which is probably of significance is delayed blanching of the extremity on elevation. This delay in the drainage of blood from the foot may well be due to venous constriction and probably indicates concommitant arterial constriction, which sympathectomy is designed to relieve.

The vasodilatation test, as commonly performed, may not allow sufficient time for the blood vessels to dilate to their maximum capacity. This fact is suggested by the frequency with which it is noted that the rise in surface temperature following lumbar ganglionectomy exceeds the highest level obtained

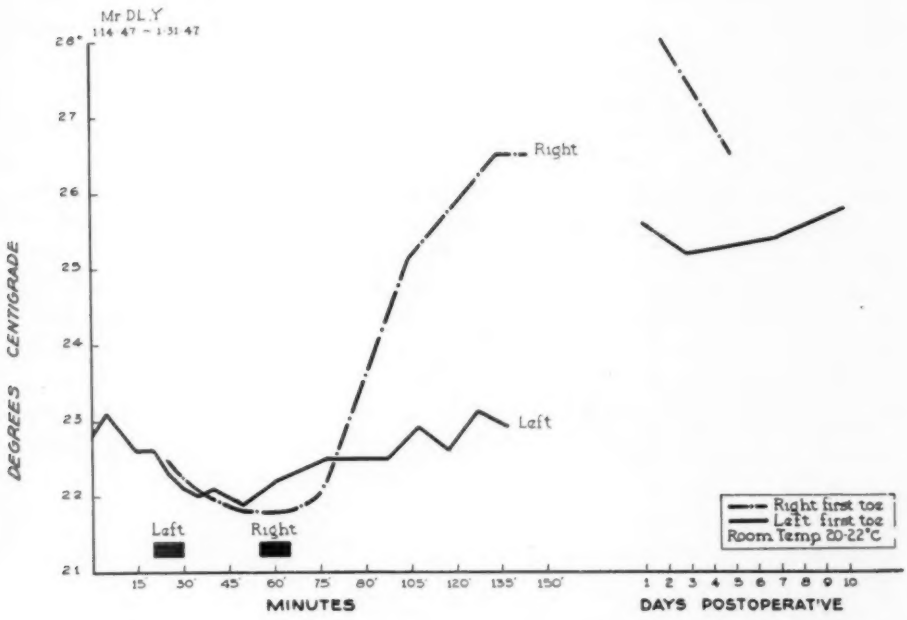

FIG. 3.—Skin temperature increase following lumbar sympathetic blocks and lumbar sympathectomies in a patient with thromboangiitis obliterans.

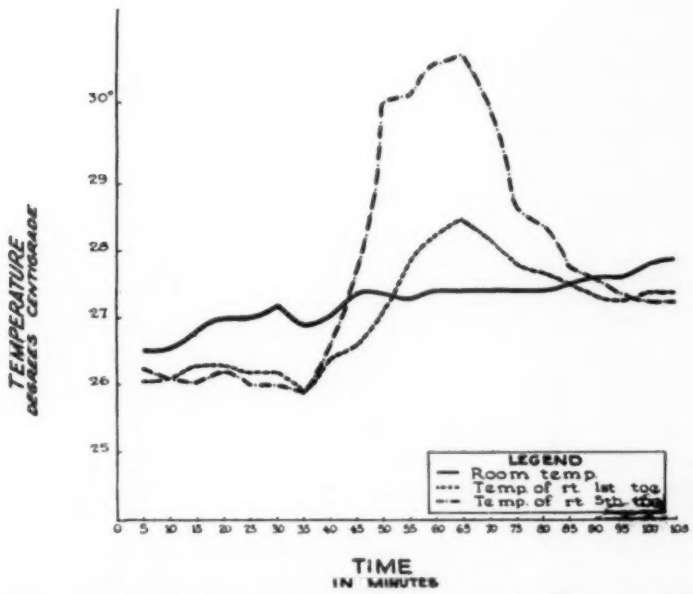

FIG. 4.—Skin temperature changes following right lumbar sympathetic block in patient with erythrocyanosis frigida.

during the vasodilatation test. Figure 3 shows the skin temperature increase following lumbar blocks in a patient with severe thromboangiitis obliterans. It can be seen that in the days following lumbar sympathectomies, the surface temperatures consistently exceeded those observed at the height of the vasodilatation tests. Subsequent studies on this patient have confirmed the value of the operations. We have come to place great reliance upon the subjective improvement, noted by the patient after temporary removal of vasomotor control by blocking the sympathetic ganglia with procaine, as an indication for sympathectomy. The indications for sympathectomy and the results obtained in a small group of patients with obliterative arterial disease are shown in Table I.

Failure of the skin temperature to increase to normal levels through vasodilatation after release of vasomotor tone does not necessarily indicate that the vasomotor tone is low. The arterial obstruction may be of such severity that it is impossible, even with the opening up of collateral channels, to deliver sufficient blood flow to the distal parts of the extremity to raise the surface temperature to normal levels. On the other hand, vasoconstriction may further reduce the circulation to the tissues. Previously, many patients were excluded from the benefits of sympathectomy, because of the failure of the surface temperature to reach normal high levels following temporary interruption of vasomotor control. In the case illustrated in Figure 4, the patient had suffered from erythrocyanosis frigida of both lower and upper extremities for many years. She developed a painful ulceration beneath the nail of her right great toe, which failed to heal in four months. Immersion of the forearms in hot water (Landis-Gibbon test) failed to produce any rise in the temperature of the toes. Blocking of the posterior tibial nerve with 2 per cent procaine resulted in a rise in skin temperature of only 2 degrees centigrade. With lumbar sympathetic block, as shown in Figure 4, the skin temperature increase was more pronounced and there was great improvement in the color of the extremity, as well as relief from pain. Bilateral lumbar sympathectomy subsequently performed, resulted in complete relief of her symptoms.

The quantity of blood which can be delivered to the peripheral tissues in a given period of time depends not only upon the diameter of the arteries supplying the part, but also upon the peripheral resistance. Lowering of the peripheral resistance in any section of the vascular bed proximal to the nutrient capillaries, especially those in the distal portions of the extremities, necessarily reduces the effective pressure. The effect upon the height of oscillations measured at the ankle of lowering the peripheral resistance by opening up of blood vessels in the working calf muscles has been previously reported. This resistance was shown to be a significant factor in the distribution of blood to the peripheral tissues. It was suggested at that time that extensive sympathectomy might be contraindicated in the presence of advanced obliterative arterial disease, since the peripheral resistance might be so lowered in the proximal portion of the limb as to curtail the flow of blood in the more distal parts of the extremity. Atlas[9] has shown that in three patients lumbar sympathectomy allowed a rise in the surface temperature of 2 to 5 degrees centigrade above

TABLE I

INDICATIONS AND RESULTS OF SYMPATHECTOMY IN OBLITERATIVE ARTERIAL DISEASE

Case No.	Patient	Age	Diagnosis	Condition of Extremity	Lowest Palpable Artery	Indications for Sympathectomy	Operation	Results	Late Improvement
1	P.A. Male U.C.H. 124118	48	T.A.O. 10 mos.	1. Spontaneous amputation of distal phalanx of 6 fingers and sclerodactylia of all fingers. 2. Tips of fingers show painful ulcers. 3. Numbness and tingling of toes.	1. Arteriogram shows rt. radial blocked and blocks of digital arteries. 2. Ankle pulses present bilaterally.	1. Cold, clammy extremities. 2. Improvement in arteriogram after lumbar sympathetic block.	1. Bilateral upper thoracic sympathectomy. 2. Bilateral lumbar sympathectomy. (L-1, 2, 3, 4.)	1. Stumps of fingers healed completely. 2. Pain, numbness and tingling of feet have ceased.	++
2	O.L.Y. Male U.C.H. 136430	49	T.A.O. 7 wks.	1. Cold, aching feet bilaterally. 2. Weakness and dragging left foot. 3. Intermittent claudication, lf. foot, 1 block. 4. Spotty ischemic neuritis.	1. Lf. popliteal. 2. Rt. dorsalis pedis (rt. post. tibial absent). 3. Rt. ulnar obliterated.	1. Cold, clammy ex tremities. 2. Moderate venous constriction. 3. No improvement in claudication with lumbar sympathetic block, but color improved.	1. Bilateral lumbar sympathectomy. (L-4 only.)	1. Coldness and aching pain gone. 2. Improvement in strength, lf. foot. 3. Claudication time improved x 20. 4. Spotty ischemic neuritis decreased greatly and finally disappeared.	+++
3	O.M. Female U.C.H. 131147	47	Raynaud's with considerable local arterial obliteration 10 yrs.	1. Erythrocyanosis frigida, upper and lower extremities. 2. Extreme cyanosis rt. large toe with ulceration.	1. Ankle pulses present bilaterally.	1. Cold, clammy cyanotic extremities. 2. Venous constriction with delayed blanching time. 3. Improvement with lumbar sympathetic block (good color, warmth and relief of pain).	1. Bilateral lumbar sympathectomy. (L-2, 3, 4.)	1. Improvement in color, warmth and pain 2. Ulcer healed.	+++
4	W.S. Ma'e Franklin 2321	52	Arteriosclerosis obliterans. 9 mos.	1. No excoriation, some rubor. 2. Colder rt. extremity. 3. Numbness of toes 3, 4, 5 on rt. 4. Intermittent claudication, rt., 1 block.	1. Rt. femoral. 2. Lf. posterior tibial.	1. Cold, clammy rt. foot. 2. Delayed blanching time. 3. Claudication improved after lumbar sympathetic block on 2 occations.	Rt. lumbar sympathectomy. (L-1, 2, 3.)	1. Rt. foot warmer. 2. Claudication time improved x 4. 3. Numbness in toes disappeared.	++
5	F.Z. Female Franklin 1998	44	T.A.O. 15 yrs.	1. Lf. foot colder than rt. 2. No ulcers.	1. Lf.: No femoral. 2. Rt.: All ankle pulses present. Radial and ulnar pulses diminished.	1. Mottled, cyanotic skin. 2. Delayed blanching time. 3. Hands moist. 4. Temporary improvement following lumbar sympathetic block.	Rt. upper thoracic sympathectomy. Lf. lumbar sympathectomy.	1. Claudication greatly improved in lf. leg and foot. 2. Claudication time improved x 5. 3. Rt. hand warmer with good circulation.	++

TABLE I—*Continued*

INDICATIONS AND RESULTS OF SYMPATHECTOMY IN OBLITERATIVE ARTERIAL DISEASE

Case No.	Patient	Age	Diagnosis	Condition of Extremity	Lowest Palpable Artery	Indications for Sympathectomy	Operation	Results	Late Improvement
6	E.K. Male Franklin 1946	26	T.A.O. 3 yrs.	1. One sq. cm. area of gangrene, rt. index finger. 2. Stasis of index with elevation and delayed filling with dependency.	1. Lf. ulnar weak.	1. Raynaud's phenomena at onset. 2. Cold, clammy extremities.	1. Rt. upper thoracic sympathectomy.	1. Increased warmth rt. arm and hand. 2. Healing of ulcer.	+
7	J.L. Male S.F.H. 38132	34	T.A.O. 10 yrs.	1. Lf. 4th and 5th toes missing with draining ulcers at site. 2. Rt. foot cyanotic.	1. Rt. leg: Pulses all present but diminished. 2. Lf. leg: Popliteal.	1. Cold, moist cyanotic feet.	1. Bilateral lumbar sympathectomy (L-2, 3, 4).	1. Ulcerated areas healed rapidly. 2. Foot and leg warmer. 3. Exercise tolerance increased x 10.	++
8	A.G.G. Female S.F.H. 40320	14	Post-traumatic spasm of brachial artery with thrombosis.	1. Pulses absent lf. upper extremity. 2. Lf. forearm and hand cyanotic, cold and anesthetic. 3. Induration of lf. forearm muscles.	1. Lf. axillary.	1. Cold, cyanotic hand. 2. Volkmann's contracture. 3. Improvement with stellate sympathetic block.	1. Left thoracic sympathectomy.	1. Return of pulses. 2. Hand still cold and anesthetic. 3. Volkmann's contracture.	±
9	H.L. Male Franklin 4172	65	Arteriosclerosis obliterans 1 yr.	1. Feet cold and moist. 2. Intermittent claudication, lf., 2 blocks.	1. No pulses below femorals.	1. Cold, clammy feet. 2. Venous constriction with delayed blanching time. 3. Improvement in color and temperature with lf. lumbar sympathetic block.	1. Left lumbar sympathectomy (L-1, 2, 3, 4).	1. Left foot warm and dry.	+
10	D.P. Male Franklin 4123	68	Arteriosclerosis obliterans 1 yr.	1. Feet cold and moist. 2. Intermittent claudication, rt., 1 block.	1. Femoral.	1. Cold, clammy feet. 2. Delayed blanching time. 3. Improvement in color and temperature with rt. lumbar sympathetic block.	1. Right lumbar sympathectomy (L-1, 2, 3, 4).	1. Right foot warm and dry.	+

the control level, but was followed by the rapid development of gangrene, necessitating amputation of the leg in each case. He attributed this disaster to the opening up of the arteriovenous communications which, although it permitted the surface temperature to rise, actually resulted in still further reduction in the nutrient capillary flow.

At approximately the same time that Atlas reported his experiences, one of us had noted some curious phenomena in four cases, the significance of which was not then appreciated. The first patient was suffering from thromboangiitis obliterations and had sustained an occlusion of the left iliac artery. Immediately following lumbar ganglionectomy the hypesthesia of the left foot, presumably of an ischemic nature, became much more extensive. At the time it was thought that the drop in blood pressure during spinal anesthesia and the use of the head-down position to combat this complication accounted for the manifest increase in vascular insufficiency. Some months later, however, he developed extensive gangrene of the dorsum of the foot, as shown in Figure 5, and amputation of the leg was performed. The fact that he continued to smoke and presumably had further episodes of arterial obliteration served to explain the development of gangrene, although the distribution of the necrosis on the dorsum of the foot while the toes were still viable was curious. Atlas described a similar distribution of gangrene in his cases.

FIG. 5. — Necrosis of tissues on dorsum of foot in patient with advanced thromboangiitis obliterans after lumbar sympathectomy.

The second patient was suffering from severe ischemic neuritis after an acute arteriosclerotic occlusion of the left popliteral artery. When she obtained relief from pain with lumbar block, the sympathetic ganglia were excised. The spontaneous pain which she had suffered constantly for 10 months was immediately relieved. However, oscillations at the ankle, which before sympathectomy were barely perceptible, instead of being improved, actually disappeared. The records obtained on this patient are shown in Figure 6. Necrosis of the tissues on the dorsum of the foot developed as can be seen in Figure 7, necessitating amputation of the leg three months later. The data on these four cases are given in Table II. None of these patients gave clinical evidence of increased vasomotor tone, but in each one there was temporary relief of severe rest pain following lumbar block. It is interesting to note that each of these patients had sustained an acute occlusion of a major artery, as the result of thrombosis. The terrific pain and hypersensitivity which they developed in the months following the acute occlusions might well have been due to ischemic neuritis or to some type of causalgia. In each case the relief of pain by lumbar block might better have been attributed to interruption of the sympathetic

impulses, which is recognized to be effective in treatment of causalgia, rather than to any improvement in the supply of blood to the peripheral tissues.

Atlas[9] has enumerated as specific contraindications to sympathectomy, 1. Severe extensive arterial occlusion; 2. Rapid blanching on elevation; and 3. Atrophy of skin and subcutaneous tissues. From our present understanding, we would now classify the cases described above as belonging to the low vascular tone group in which specific indications for sympathectomy were not present. Moreover, they presented signs which we now regard as specific contraindications to sympathectomy.

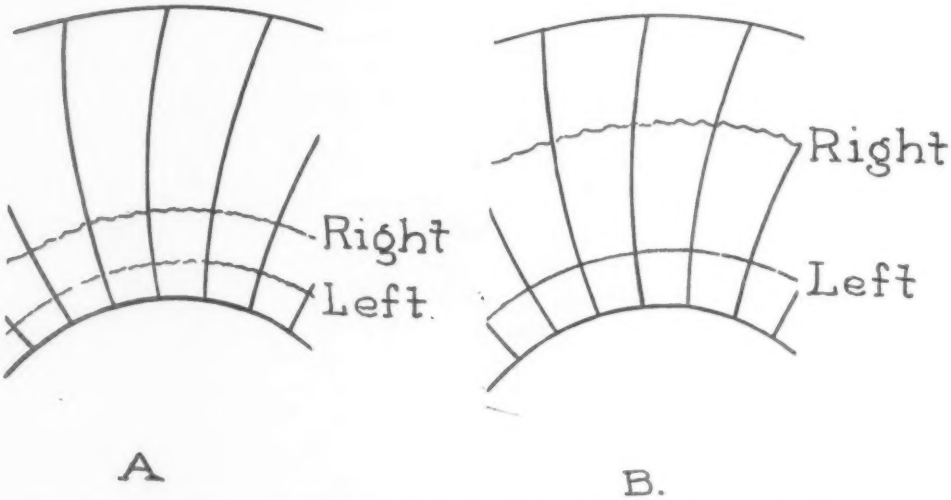

FIG. 6.—Simultaneous arteriograms in a patient with thromboangiitis obliterans after left lumbar sympathectomy.

The gangrene following sympathectomy in patients with severe obliterative arterial disease may be likened to the gangrene which so frequently follows proximal ligation of the major artery in the presence of an arterio-venous fistula. Direct measurements of intra-arterial pressure[15] have shown that occlusion of the major artery proximal to an arterio-venous fistula results in a precipitous drop of pressure due to the greatly expanded vascular bed available on the venous side. Arterial blood brought down by collateral pathways escapes easily into the venous side of the circulation. In obliterative vascular disease the major arteries are already blocked. Destruction of vasomotor control over the arterio-venous anastomoses by sympathectomy may abruptly deflect into the venous system the nutrient collateral flow to the capillaries. Clark[4] has shown that, with both the capillaries and the arterio-venous anastomoses open, there is blood available to flow through both pathways, although the relative size of the arterio-venous shunts allows far greater diversion of blood to the veins directly than through the capillaries. It is interesting to speculate on what would be the case were the volume flow of blood to be reduced by compression of the afferent arteries while the arterio-venous anastomoses were open.

TABLE II*

CONTRAINDICATIONS AND RESULTS OF SYMPATHECTOMY IN ADVANCED OBLITERATIVE ARTERIAL DISEASE

Case No.	Patient	Age	Diagnosis	Condition of Extremity	Lowest Palpable Artery	Reason for Sympathectomy	Operation	Result	Contraindications to Sympathectomy
1	L.B. Male H.U.P. 43202	45	T.A.O. Sudden occlusion lf. iliac artery.	Numb foot with constant burning pain.	None on lf.	1. 4° C. rise in skin temp. after nerve block.	Lf. lumbar symp. L-1, 2, 3, 4.	Immediate increase in anesthesia. Necrosis dorsum of foot. Amp. of leg 18 mos. later.	1. Absent oscillations at ankle. 2. Pain due to "ischemic neuritis." 3. Continued smoking.
2	E.L. Female Grad. Hosp. 149471 H.U.P. 47754	54	Arteriosclerosis. Sudden onset blanching and coldness lf. foot	Tender, thrombosed popliteal artery. Foot warm, hypersensitive.	Femoral	Relief of pain by lumbar block.	Lf. lumbar symp. L-1, 2, 3, 4.	Immediate relief of pain. Necrosis dorsum of foot. Amp. of leg 3 mos. later.	1. Atrophy of soft tissues. 2. Pain due to "ischemic neuritis." 3. Rapid blanching on elevation.
3	M.B. Female H.U.P. 45979	59	Diabetes. Arteriosclerosis. Sudden occlusion lf. femoral artery.	Foot warm but hypersensitive.	Femoral	Relief of pain by lumbar block. Temporary relief from periarterial sympathectomy.	Periarterial symp. femoral artery. Alcohol injection. L-1, 2, 3.	Ecchymosis dorsum of foot. Amp. of leg 12 mos. later.	1. Absent oscillations at ankle. 2. Pain due to ' ischemic neuritis." 3. Rapid blanching on elevation 15 sec.
4	M.B. Male P.H. 58148	58	T.A.O. Post-traumatic causalgia.	Fracture 1-2 metacarpals. Ulceration 3rd toe. Foot warm, hypersensitive.	Femoral	Previous femoral periarterial sympathectomy with temporary improvement. Relief of pain by lumbar block.	Lf. lumbar symp. L-1, 2, 3.	Immediate increase in ecchymosis dorsum of foot. Amp. of leg 2 mos. later.	1. Atrophy of soft tissues. 2. Pain due to "Causalgia." 3. Rapid blanching on elevation.

* We desire to express our appreciation to the following hospitals for permission to use the records from their surgical services: Hospital of the University of Pennsylvania, Graduate Hospital of the University of Pennsylvania and the Pennsylvania Hospital.

FIG. 7. — Necrosis of tissues on dorsum of foot 3 months after lumbar sympathectomy in patient with arteriosclerotic occlusion of popliteal artery.

The question may be raised as to how sympathectomy produces its admittedly good results if the only effect is the opening up of the arterio-venous communications. In the first place, the best results from sympathectomy are obtained in those patients who have capacity for vasodilatation and especially in those in whom there is a high degree of vasomotor tone. The possibility that the vasomotor tone restricts the blood flow to the tissues is suggested by the objective improvement in muscle blood flow which obtains after release of vasomotor control.[14] It is quite likely that even the major arteries are under vasomotor control. Arteriographic studies on three patients before and after either temporary paralysis of the sympathetic vasoconstrictor nerves or lumbar sympathectomy demonstrated an increase in the volume flow of blood through the major arteries. Figure 8 illustrates the results obtained in a patient with thromboangiitis obliterans after left lumbar sympathectomy. The ankle pulses were present on both sides but after release of vasomotor control on one side the flow of blood through the major arteries was greatly increased.

It is well known that the presence of a fistula between the major artery and vein of a limb is an excellent stimulus for the development of collateral circulation. Arteriographic studies in patients with arterio-venous fistulas demonstrate the profuse development of such collaterals. The fact that quadruple ligation and excision of such fistulas is rarely followed by gangrene indicates their functional importance.

In his microscopic studies of arterio-venous anastomoses, Popoff[7] called attention to the frequency with which the afferent artery became dilated. It is possible that the benefits of sympathectomy may actually be attributed to the permanent opening of multiple small arterio-venous communications. Such arterio-venous fistulas furnish a stimulus for the dilatation of afferent arteries and collateral channels. Atlas[9] has demonstrated that, after a period of time following lumbar sympathectomy, there appears to be an actual hypertrophy of the collateral bed, allowing for an increase in the oscillations compared with those taken immediately after operation.

Although the peripheral circulation has a dual function with dual control and even a dual microscopic structure, the blood supply comes through one system of arteries. Removal of vasomotor tone by sympathectomy, especially in those cases in which this vasomotor tone is increased, may reasonably be expected to improve the circulation to the tissues in spite of the diversion of large quantities of blood through useless channels into the veins. In addition,

sympathectomy may not unreasonably be expected to furnish an adequate stimulus for the development of collateral circulation. In the presence of severe obliterative vascular disease, however, especially in those cases with low vasomotor tone, sympathectomy may be contraindicated because large quantities of

FIG. 8.—Oscillometric records taken at the ankle before and after lumbar sympathectomy in patient with arteriosclerotic occlusion of the popliteal artery.

blood are diverted directly into the veins without passing through the capillary system.

CONCLUSIONS

Sympathectomy is useful in the treatment of obliterative arterial disease, especially in those patients who show evidence of abnormal vasoconstriction. Even though preoperative diagnostic tests fail to show an adequate rise in skin temperature after release of vasomotor control, sympathectomy may bring about a lasting and progressive improvement.

In advanced obliterative arterial disease, however, especially in patients without evidence of abnormal vasoconstriction, sympathectomy may result in gangrene. Although the total circulation may be increased after sympathec-

tomy in these cases, much of the blood is probably shunted directly into the veins through the opening-up of numerous arterio-venous anastomoses. The nutrient capillary flow may actually be reduced.

In the less advanced cases of obliterative arterial disease, sympathectomy may promote the development of collateral circulation through permanent opening of these arterio-venous communications.

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DISCUSSION.—DR. LOUIS G. HERRMANN, Cincinnati: Doctor DeBakey has presented in modern dress another important factor in the maintenance of peripheral blood flow under various conditions. For decades physiologists have tried to impress upon us the importance of the shift of the mass of blood from one part of the body to another when certain physiologic needs are to be satisfied. The sleepiness which comes on after a hearty dinner, the cerebral ischemia which sometimes overtakes a speaker when he reaches the rostrum, the muscle cramps in extremities which come on when one goes swimming immediately after a heavy meal, are all practical examples of the shift of the mass of blood from one part to another as a result of the vasomotor function of the sympathetic nervous system.

Doctor DeBakey and Doctor Ochsner have chosen to call this the lending-borrowing mechanism, but I prefer to describe it by the term "hemometakinesia" which they have coined. I am also of the opinion that such a mechanism is of real importance and I would emphasize that such a shift of the mass of blood should be given serious consider-

ation in all patients who are to be subjected to sympathetic denervation of any part of the body.

It is encouraging that vascular surgeons are also returning to the study of the fundamental physiology of the peripheral circulation and, as we have heard this morning, a better understanding and better therapy of peripheral vascular disease is our ultimate objective. The effects of local tissue hypoxia and anoxia have interested me greatly for several years and it is our hope that we may sometime add a little information about this important factor. The secondary development of venous or arterial thrombosis in patients with peripheral vascular diseases might be the deciding factor in the success or failure of any of the therapeutic agents which we employ in the management of these important clinical conditions.

Now I should like to discuss for a few minutes some of the applications of the timely studies of Doctor Freeman and his associates. It is my opinion that the operation of sympathetic ganglionectomy should not be looked upon as an innocuous procedure, particularly in patients with extensive structural changes in the peripheral arteries, since widespread denervation has been shown even to precipitate gangrene of the tissues. So far as I can determine, there is no positive evidence to show that sympathectomy does any more than relieve the increased vasomotor tone in the arterial bed and cause the opening of the arteriovenous communications of Sucquet and Hoyer in the skin. Doctor Freeman has emphasized that after sympathectomy the real stimulus to the development of a collateral arterial circulation might come directly from the opening of these small intradermal arteriovenous communications. I can only re-emphasize the fact that in patients with extensive structural changes in the peripheral arterial system unassociated with increased vasomotor tone, sympathetic denervation of the part should not be performed because the opening of the arteriovenous communications in the skin will divert large quantities of blood directly into the veins and thus reduce the nutrition of the tissues to an even lower level.

We have been interested in the effects of therapeptic measures upon the collateral arterial circulation. Doctor Freeman has already stated that sympathectomy only favors the development of a collateral arterial circulation. The flow of blood to the extremities and the exchange of blood in the capillaries, follow definite physical laws, and the importance of these factors must not be overlooked in any consideration of this kind. The flow of blood is equal to the pressure in the vessels divided by the peripheral resistance. About ten years ago we presented before this Association a physical means of increasing the flow of blood through the peripheral arteries and capillaries in patients with obliterative disease. We designated this type of treatment as "Passive Vascular Exercises." Conclusive evidence has been presented to show that the alterations of the environmental pressure about an extremity actually promote the flow of blood through existing collateral arteries. When properly used, passive vascular exercises serve as a valuable adjuvant in the management of arterial insufficiency due to structural changes in the arteries of the extremities.

Doctor Freeman's message should make us all give the problem of sympathectomy for obliterative arterial disease further serious thought and study. Such studies as these should stimulate us to give our patients the benefits of all other adjuvants which have been shown to be effective in increasing the peripheral flow of blood in such patients. Until we learn more about tissue metabolism following sympathectomy, as well as the other methods of increasing the peripheral flow of blood to tissues, we will not be able to predict accurately the effect of any of our therapeutic procedures in patients with obliterative arterial diseases.

DR. H. T. BALLANTINE, JR., Ann Arbor, Mich.: Studies in progress at the University of Michigan are pertinent to Doctor Hermann's excellent discussion. Briefly, they consist of measuring peripheral blood flow in the lower extremities of normal individuals at rest and again under three varying conditions: (1) After intravenous injection of tetra-ethyl-ammonium chloride 500 mg., producing ganglionic blockade of the autonomic nervous system. (2) After lumbar sympathetic block of one lower extremity and, (3) after injec-

tion of 500 mg. of TEAC while lumbar block is still effective. Measurements of blood flow through the foot have been obtained with the venous-occlusion water plethysmograph technic. Skin temperatures have been recorded by means of the Leeds-Northrop potentiometer where feasible. Environmental temperature has been stabilized at 68 to 70° F.

The following slide is typical of our findings:

1. Lumbar block produces a rise in peripheral blood flow and in skin temperature.
2. Intravenous TEAC does not decrease the blood flow obtained by block.
3. The blood pressure was not significantly altered in these normal subjects.
4. Intravenous TEAC produces an increase in peripheral blood flow. It causes as well a rise in skin temperature equivalent to that obtained by block. This would indicate that TEAC produces a significant rise in peripheral blood flow even though the flow obtained by block is greater.

From these observations it would seem that TEAC produces a marked increase in peripheral blood flow to an extremity, despite its generalized vasodilating effect. These results have been verified in a series of 62 patients, 57 of whom showed increased flow after injection of this drug alone. This may be explained on the basis of increased cardiac output which maintains an adequate head of pressure in the arterial tree. Our ballistocardiographic studies have shown that cardiac output may rise from 10 per cent to 20 per cent after intravenous injections of tetra-ethyl-ammonium chloride.

Although changes in skin temperature are relatively the same in both procedures, there is greater increase in blood flow to an extremity with sympathetic nerve block than with TEAC. The preservation of the lending-borrowing mechanism with local block might be given as an explanation. It does not, however, fit our findings that increased blood flow to the foot produced by paravertebral sympathetic block is not decreased by an injection of TEAC. These results indicate that generalized vasodilatation and possible abolition of the lending-borrowing mechanism does not inhibit increased blood flow to a local part, provided cardiac output can be increased sufficiently to maintain arterial pressure.

A more probable explanation for the disparity between the increase in blood flow after block and after injection of TEAC is that in 500 mg. doses the drug does not produce complete autonomic block.

Dr. I. Ridgeway Trimble, Baltimore: Doctor Freeman's paper is most timely in pointing out the pitfalls that may be encountered in surgery of the vascular diseases. Some years ago, before the war, we wrote about some of these cases in which the tests were not conclusive; yet beneficial results did follow operation. This has been borne out by DeTakats, who says he is in agreement, and he is now submitting patients to operation who, according to tests, were formerly considered unsuitable. I have never encountered gangrene of the extremity following lumbar sympathectomy.

Doctor DeBakey's paper is most interesting. Hematokinesia—the borrowing-lending mechanism, better known as Greco-Turkish mechanism of lend-lease. We have recently used this principle of borrowing blood for a double purpose; to prevent shock at the time of operation and to decrease the incidence of postoperative thrombosis.

The skin surface of the lower extremities comprises 38 per cent of the total body surface. It is the blood from this large area that we wish to borrow for use elsewhere.

Dr. David Lynn and I are now investigating the possibility of lowering the incidence of postoperative thrombosis and thrombophlebitis by binding the lower extremities with elastic bandages during operation and by keeping these bandages in place after operation for a period of two weeks. We are at present conducting studies on the blood flow in the deep veins of the lower extremities after the application of these bandages.

Dr. D. W. Gordon Murray, Toronto: I should like to comment on the papers of Doctor Smith and Doctor Blakemore. Doctor Smith in his paper described using plastic

tubes for anastomosis. I would like to ask Doctor Smith if he lined the tubes with a venous graft or was the anastomosis done with the plastic material only.

Regarding Doctor Blakemore's paper, I admire the way he puts this damaged artery together. My own predilection would be for suture, but that is a weakness on my part. The maintenance of circulation after either graft or suture, I think, is the main thing to be obtained. The main thing is to provide circulation to the area involved. In my hands, by giving heparin I can be more certain to maintain the patency of the anastomosis.

In one of the animals' hearts shown yesterday, removed from an animal in which we had done a vein graft in a carotid artery nine years previously, the vein graft was removed at this time. Its lumen was patent. It was slightly larger than the adjacent artery. The wall in some places was rigid so that it fractured when it was opened out. I am not sure whether it was calcium or bone. Further investigation of this will be made and sections made to determine just what are the changes in this venous graft after nine years functioning in an artery.

In a clinical case, a boy in whom a 2.5 inch graft of vein was placed in the femoral artery eight years ago, this has been working well ever since. There is no sign of aneurysm. On palpation it does not feel rigid or stiff. It seems to be functioning satisfactorily.

There probably is a place for venous grafts in arteries under suitable conditions.

DR. PETER HEINBECKER, St. Louis: I want to discuss Doctor DeBakey's paper, and to ask Doctor Ballantine a question. The alteration of blood flow to organs and tissues in response to need is a dynamic phenomenon dependent on nervous, humoral, local metabolic and thermal influences. Of these the accumulation of local metabolites probably is of first importance. It is not necessarily dependent on the sympathetic nervous system for its initiation or continuance. This is supported by evidence of its adequate functioning in the denervated extremity. Of the important humors, none is more so than epinephrine, which serves to decrease the blood flow to the skin and the splanchnic area while increasing that to the muscles, the brain and the heart. For the release of epinephrine the sympathetic nervous system is essential. The nervous influences which modify blood distribution are reflexly initiated. They serve particularly in the maintenance of a stable blood pressure and a normal body temperature. In special situations nervous influences modify secretion rapidly in response to need, a function later taken over in large measure by humors or enzymes.

The temporary increase in the size of a portion of the vascular tree effected through denervation is a static phenomenon, not to be confused with the dynamic processes involved in blood distribution occurring spontaneously to meet changing metabolic requirements.

I was much interested in Doctor Ballantine's statement that tetra-ethyl-ammonium chloride causes a block in the ganglia of the autonomic nervous system. I would like to know what evidence he has of such a block.

DR. WALTER G. MADDOCK, Chicago: I would like to comment first on the paper of Doctor Freeman. It has been pointed out before that the skin temperature response of the hands and feet to an increased environmental temperature or to a sympathetic or peripheral nerve block is greatest in the normal individual, for his unobstructed vessels can dilate to the maximum. From work done with Doctor Coller at Michigan the old theory was re-emphasized that the arms and legs, particularly the hands and feet, play a very important part in the dissipation of heat from the body, being the areas of greatest variation in superficial blood supply in response to heat production versus the environment into which the heat has to be dispersed. The hands and feet act in the same way as the radiator of an automobile. The engine block gives off heat, like the body, but the shunt of water to the radiator is the main variant as the need for heat dissipation varies. Doctor Freeman has shown again the arteriolar-venous shunt system in the fingers and toes, which un-

doubtedly is a part of the mechanism for passing more blood through these areas when there is a need for more heat dissipation. With the greatest responses in the normal, one must be careful then to not interpret all increases in peripheral skin temperature as a result of test procedures as an overcoming of "vasospasm." Much of the temperature increase is due to an overcoming of vasoconstriction which is a normal part of the heat dissipating mechanism. In actual practice one often does not need to test for vasospasm but can see its presence by sweating or multiple color changes in the part.

So far as sympathectomy is concerned, particularly for the lower extremities, it is a relatively simple procedure now and I place it under the heading of conservative treatment. Patients with a peripheral vascular deficiency from arteriosclerosis are debilitated and disabled just as much as a cardiac patient, and every method must be used to improve the blood supply to the legs and feet. A slight gain may be sufficient to enable them to carry on for months or years without trouble. And since gangrene is such a common end result in all patients with serious peripheral vascular deficiency, it is difficult to be certain that in some way the sympathectomy caused or hastened this death of tissue. I do not believe that Doctor Freeman is advising that we abandon sympthectomy for many of these patients.

Doctor DeBakey's paper on "lending-borrowing" blood from the body proper to the extremities in cases of need is interesting. The lending-borrowing should be brought about in the conservative management of all cases of a peripheral vascular deficiency. If normal individuals keep their trunk warm by wearing woolen underwear, then more blood will be sent to the hands and feet for the dissipation of heat. Patients with peripheral vascular deficiency as a result of peripheral arteriosclerosis or Buerger's disease should be instructed to keep the body warm at all times, to wear woolen underwear and woolen socks if necessary, for more blood will then be sent to the extremities. Such patients in the hospital should be kept extra warm, not just comfortably so: the body should be warmer than usual, to a point a little short of sweating. Extra blankets should be supplied, or a heat cradle placed over the abdomen, not over the feet. An electric pad to the abdomen will also add general heat, and one of the new electric blankets is a suggestion. In contrast to many other forms of treatment, such environmental therapy sending blood to the extremities can be used in the hospital for 24 hours a day, an essential time period to combat the disease and disability of peripheral vascular deficiency.

Dr. Frank B. Berry, New York: I would like to discuss Doctor Smith's paper and to add our own experience. We were fortunate in having some experience behind us, so that when the Seventh Army prepared to go into France we sent out a directive requesting that all major injuries of arteries be listed. We had 1086 such cases.

Further amputations undoubtedly were necessary in the general hospitals, but we urged that all such injuries be held in forward hospitals until the outcome was known. Our femoral artery injuries are not subdivided but are dealt with as a group. We had 190 cases, 90 amputations; we had 179 popliteal injuries, 125 amputations. In Tunisia, for example, the Ninth Evacuation Hospital had nine injuries of the popliteal artery, resulting in 100 per cent amputations. In France they had three consecutive cases with no amputations. That is how these injuries varied as to outcome. Much depended on the type of wound, extent of soft part damage, coexisting fractures, time elapsed between wounding and surgery, etc.

We did use some heparin and we considered that it helped. We used glass and plastic tubing, and some of the hospitals had Blakemore cuffs and used grafts. We believed these were all helpful when it was possible to use them.

It has been advocated in the case of elderly people in whom there is lessened arterial supply to the leg, that a bilateral sympathectomy be performed. Doctor DeBakey's lending and borrowing mechanism may suggest that. We know that these people are prone to go on after sympathectomy has been performed on one side to develop gangrene in the other leg, and we wonder in these cases if a bilateral sympathectomy may not be indicated.

DR. ALTON OCHSNER, New Orleans: My remarks will be limited to a discussion of Doctor Freeman's paper. I am sure that Doctor Freeman did not wish to leave the impression that older patients with arterial disease should not be given the advantage of sympathectomy. We have become increasingly more impressed by the desirability of resorting to sympathectomy even in older persons who have obliterative arterial disease and, although in not all of these patients can the extremity be salvaged, the salvage incidence is about 75 per cent, which makes the procedure justifiable. We have also learned that the results obtained by temporary blocking of the sympathetic nerves by novocaine will not give a true indication of what can be obtained by sympathectomy in these older individuals. We have had considerable experience with sympathectomies in older individuals with obliterative arterial disease, and in only one instance have we observed a gangrene which apparently became progressive after the sympathectomy. We believe that this was coincidental and that the sympathectomy was not in any way associated with the gangrene but that the gangrene occurred in spite of the sympathectomy. There are many other patients in whom gangrene has been prevented by a sympathectomy. It seems to us that to deny an older patient any procedure which will increase his chance of maintaining a viable limb would be extremely undesirable.

DR. WILLIAM F. MACFEE, New York: Doctor Smith's observations on the treatment of injuries of major arteries during the war are impressive. It is obvious that they represent the general experience of World War II. It is also evident from his report and other records that current methods of restoring continuity of severed vessels, while occasionally successful, have not been sufficiently so to materially alter results. I do not believe we can claim that the results of new methods, which include the bridging of defects between severed ends, are superior to the older procedure of simple ligation.

The failures no doubt have been due in part to defects in the methods employed, but perhaps in greater measure to the character of the wounds. The energy, or in this case the destructive force of a missile, varies directly with its mass and with the square of its velocity. The destruction of tissue produced by the modern high velocity bullet or shell fragment is enormous. An artery is not simply cut, but as a rule a segment is torn out and a large area of surrounding parts, including the collateral circulatory system, is reduced to a pulplike state and completely devitalized. In addition to the local wound, frequently there are other grave wounds of the same extremity or of other parts. Under such circumstances, it is not surprising that so many limbs are lost, but rather that something like 50 per cent are saved.

To obtain better results it is evident that better methods of repair must be found. A serious disadvantage in dealing with war wounds is the impracticability of using the anticoagulants. Doctor Berry has described a case of delayed hemorrhage which illustrates the danger of interfering with the clotting mechanism in the presence of extensive wounds. Unless better methods of local hemostasis can be found, it would appear that any reliable method of restoring the continuity of major arteries interrupted by war wounds must preclude the use of anticoagulants.

DR. FREDERICK L. REICHERT, San Francisco: Perhaps I did not understand Doctor Smith, but in the last war they tied off the corresponding named vein when the artery was severed. I do not know why that was not done in this war.

That case of gangrene Doctor Freeman showed I think is due to thrombosis of the femoral vessels, and has nothing to do with sympathectomy. If you want to treat these people with impaired circulation you should consider the entire atreriosclerotic condition. I consider five extremities, including the head, and you have to keep that as warm as you do the legs and arms. Sympathectomy has helped these people, up to the age of 80 or 90. I think this case of gangrene is due to thrombosis of the femoral vessels and not to sympathectomy.

DR. RUDOLPH MATAS, New Orleans: I believe that Doctor Blakemore's restoration of the main arterial channel in the aneurysmal sac by his "vein graft inlay" is a decided

step forward in the practice of conservative aneurysmorrhaphy, specially in dealing with those aneurysms in which the reliability of the collaterals is in doubt.

Despite the fact that in the majority of cases in which a pulsating hematoma has had time to develop as an aneurysmal sac, thereby assuring the establishment of a collateral circulation, and that the limb will be preserved even if the sac itself is obliterated,—the restoration of the main channel of the circulation in the sac is desirable, since it is possible that the collateral circulation may be preserved sufficiently to save the limb from an amputation, but not sufficiently to prevent secondary ischemic atrophies and other functional disabilities which leave an imperfect cure.

It is fortunate that in the vast majority of the endoaneurysmorrhaphies of the obliterative type, the collateral circulation is so little disturbed that secondary ischemic relics of the obliterative aneurysm are seldom sufficiently apparent to impair the cure. Nonetheless, it is obvious that, when the anatomic conditions within the sac are not favorable for the restorative types of endoaneurysmorraphies (Endo-A, Restorative; Endo-A Reconstructive) that the use of a Blakemore venous lined vitallium tube or a plain venous inlay with his vitallium cuffs would be a helpful and relatively simple resource.

It is well to remember that in trying to restore the continuity of the main artery in the sac of the aneurysm, the Blakemore procedure is not applicable to all type of sacs, but seems to me specially adapted to sacs in which the inlet and outlet lie in the floor of the sac in the same horizontal level, as is more frequently the case in popliteal aneurysms. It is different, however, when the artery lies on the roof of the sac and the outlet appears on the floor, or when the inlet and the outlet are eccentrically placed at different levels. To adjust a venous graft under these conditions may involve too much traumatism and handling to make the graft a success. These differences in the relation of the artery to the sac I described long ago in connection with the "Morphology and architecture of aneurysmal sacs" and in the interpretation of "Rotation in aneurysmal sacs," specially those of the popliteal space (Keen's Surgery, Vol. V, pp. 221–226).

While great progress has been accomplished within the course of the half century since I began to utilize the suture as a conservative substitute for the ligature in the cure of aneurysms—so that now the repair of injured arteries and veins has become a sort of plastic art in which many of our younger contemporaries have become great artists—I believe that we are on the way to devise still simpler methods and more handy materials than venous grafts, to bridge over gaps in the arterial stream. The distance we have travelled on the road of progress, between the Tuffier tube of the first world war and the venous lined vitallium tube of the Blakemore pattern—is quite encouraging.

Doctor Smith's study of 114 arterial wounds followed by gangrene in 54 per cent proves that the disastrous injuries of the great vessels at the front fully justify the special care and concentrated attention that the Surgeon General's office has given to these wounds in the second world war, in a supreme, but yet feeble effort to counteract the ever increasing destructiveness of the implements and materials of warfare.

Doctor DeBakey and associates and Doctor Freeman have dealt with the Surgery of the Sympathetic very interestingly, but from an entirely different viewpoint. Doctor DeBakey has opened a new field of therapy for the play of the already crowded vasomotor nerves which may soon yield a crop under Doctor DeBakey's fertile sowing.

Doctor Freeman has rendered a real service by sounding a note of alarm regarding the indiscriminate resort to lumbar sympathectomy by operation or by anesthetic block, without clear differentiation of the indications and contraindications of the procedure.

What is particularly objectionable is to resort to lumbar sympathetic block as a routine procedure before or after an operation for an aneurysm or a main artery injury in the extremities, in which there is no question regarding the sufficiency of the collateral circulation. There is, no doubt, an enormous abuse of this serious procedure, particularly when performed by inexperienced and incompetent assistants who, at best, simply perform a paravertebral novocain anesthesia. As a rule, no trouble is taken to demonstrate the effectiveness of the injection by the temperature of the dependent parts or determine, in

other ways, if the anesthetic has actually reached the ganglia. It is interesting to note in this connection that Doctor Elkin with all his large experience in aneurysmal surgery, has gotten along altogether without a single call for a lumbar block. In my experience, in over 600 operations on the surgical blood vessels, including 250 aneurysms, I have only once called for the "lumbar block" in threatened gangrene of the foot. It is more than probable that, if sympathetic lumbar block had been in vogue when I was operating, in earlier years, as it is now, I would probably have been doing Sympathectomies *a la mode*. I wish it understood that I prize sympathectomy as a precious help when it is needed, but object to it as a routine prophylactic for unthreatened gangrene.

The same protest applies against the abuse of transfusion, which is now being used as a panacea for all evils and especially as a prophylactic against shock and hemorrhage in operations in which there is no reason to expect such complications. There is no doubt that in this way much good blood is wasted, and many who are only profiteers and not patients, benefit by the procedure.

I have long trespassed upon the indulgence of the Chair and must now close with thanks to him and to the vascular surgeons who have contributed so brilliantly and profitably to the enjoyment of the Scientific Program.

Dr. Arthur H. Blakemore, New York (closing): I am deeply indebted to Dr. Rudolph Matas for discussing my paper. More than 50 years ago he presented to the profession an operative technic for the cure of peripheral arterial aneurysm that has greatly lowered the incidence of gangrene. Doctor Matas' teachings were ever before us in evolving the vein graft in lay technic. Therefore it is with some satisfaction that I present this method which does not violate his teaching in necessitating removal of the aneurysm sac, as have former methods of vein graft bridging for the restoration of blood flow.

Doctor Murray has asked about the use of heparin. We employed it postoperatively in all four cases.

Dr. M. E. DeBakey, New Orleans (closing): I should like first to express my appreciation of the stimulating discussion. In view of the political implication of the term, "borrowing-lending," it is perhaps well that a more scientific term has been proposed for this phenomenon.

I was particularly interested in Doctor Heinbecker's comments concerning cardiac output and its effect upon the changes in peripheral blood flow which we have described. It is somewhat difficult, however, for me to understand how variations in cardiac output can produce concomitantly changes of a different order in the volume of blood in such peripheral parts as the fingers and toes. In other words, I do not understand how an increase in the volume of blood in the toes associated with a simultaneous decrease in the volume of blood in the fingers may be attributed to fluctuations in cardiac output.

Doctor Ballantine's comments regarding recent studies which they have done, showing an increase in cardiac output following the administration of tetra-ethyl-ammonium chloride are also of interest. As we have indicated previously, an increase in cardiac output can produce an increase in blood flow to peripheral parts which, obviously, should be generalized. The desirability, however, of producing an increase in blood flow to a peripheral part by this means is, I think, open to question.

With regard to Doctor Berry's question concerning bilateral sympathectomy, especially in certain forms of peripheral vascular disease involving the lower extremities, we have come to employ the procedure with increasing frequency.

Dr. Morris K. Smith, Staten Island, New York (closing): In answer to the question as to whether the plastic tube was lined with vein, it was not. Some surgeons used glass tubes. Plastic tubes have the advantage of being malleable when heated. Doctor Murray has shown that heparin opens the field for arterial repair.

Doctor Berry quoted from the experience of the Seventh Army and said that doubtless many cases came to amputation after evacuation. I did not use our amputation rate in my figures because so many patients with limbs becoming gangrenous had to be sent on before we felt they were ready for amputation.

Doctor MacFee brought out a salient feature in arterial injuries of war, the widespread destruction caused by modern missiles. A reason the incidence of gangrene is so high is injury to the collateral circulation. If we are to have better results in future wars it is important to develop some means of preserving the main blood channel. Heparin will keep the anastomosis open if it can be used. It may be possible to close wounds more completely than we do in the average case in order to make heparin less dangerous.

Doctor Reichert raised the question of ligation of the accompanying vein. The data in my files are not sufficiently detailed to give an answer. It is to be remembered that when the artery is wounded the vein also is likely to be and therefore to require ligation.

Dr. Norman E. Freeman, San Francisco (closing): I appreciate very much the comments which have been made in the discussion of the place of sympathectomy in the treatment of obliterative arterial disease.

In regard to Doctor Reichert's objection, since the patients already had obliteration of their femoral arteries it is unlikely that thrombosis of the femoral vessels accounted for the gangrene after sympathectomy.

In reply to Doctor Maddock and Doctor Ochsner, we are not abandoning sympathectomy in patients of the older age group. In face, we are actually advocating an extension of this valuable procedure. We believe, however, that arterial ischemia *per se* is not an adequate indication. We think that there is a specific indication for the performance of this operation. The indication is evidence that *abnormal* constriction of the blood vessels exists. In the absence of this indication there may be specific contraindications to sympathectomy. When contraindications are present, widespread denervation of the vascular bed may actually result in harm. We have simply called attention to a possible mechanism through which the nutrient supply of blood to the tissues may be reduced by sympathectomy.

It must be emphasized that this concept is still hypothetical. Diversion of arterial blood into the veins as a result of sympathectomy still remains to be proved in patients with peripheral vascular disease. Fundamental investigations by numerous individuals have established certain mechanisms which may be involved. Such mechanisms appear to explain the unfortunate results which we have occasionally observed.

CHONDROSARCOMA*

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PHEMISTER described chondrosarcoma of bone in 1929 as a distinct clinical and pathologic entity.[11] This group of neoplasms has since been included in the classification of osseous tumors by the Bone Sarcoma Registry of the American College of Surgeons.[3] Reports of chondrosarcomas antedate Phemister's contribution but his efforts focused the attention of American surgeons and pathologists on these lesions. The 13 cases seen by us during the past 20 years not only illustrate the general characteristics of the group but also emphasize certain difficulties in pathologic diagnosis, surgical treatment and prognosis. We have also reviewed 61 cases from the files of the Bone Sarcoma Registry.

Chondrosarcomas may arise in any bone that grows by endochondral ossification. The sites most frequently involved are the ends of the femur and tibia, the proximal end of the humerus and the pelvis. These locations account for 75 per cent of the 74 chondrosarcomas we have studied.

Chondrosarcomas may arise either centrally or peripherally. They form bulky masses which invade and destroy adjacent bone and project into the surrounding soft tissues. They are among the largest neoplasms encountered. Their external surfaces may be smooth or bosselated. They look gray and feel firm although large areas may be elastic and even fluctuant, depending upon the extent of liquefaction necrosis and the amount of myxomatous tissue present. Hard areas usually indicate calcification. A part of the tumor may appear encapsulated on superficial examination but closer inspection reveals that it is merely circumscribed by distended periosteum. Infiltration of soft tissues may be seen macroscopically and atrophy of contiguous skeletal muscle is commonly found.

One usually has no difficulty in recognizing the hyalin, blue-gray translucent cartilage that is seen on cut section of most chondrosarcomas. It may be lobulated by thin fibrous septa but frequently lobulations are indistinct and sometimes, absent. Islands of myxomatous tissue appear pale and watery. Ragged, crateriform excavations filled with viscous fluid are found in some tumors. Irregular deposits of pale yellow, opaque, gritty, hard material indicate calcification, a common finding. Some of the tumors may contain relatively small fibrous appearing areas and true bone is sometimes found.

The microscopic anatomy of chondrosarcoma is extremely variable. Each tumor may mirror the complete histogenesis of cartilage, or the end product of tumor differentiation may contain only one histogenetic phase. The more cellular and more anaplastic areas are usually encountered at the periphery of the

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tumor. The center is frequently necrotic, calcified or ossified. Ovoid lacunar cells predominate in typically hyalin areas, spindle-shaped or stellate cells, in myxomatous foci. Extreme pleomorphism may characterize some tumors or parts of an individual neoplasm. Matrix may be basophilic and hyalin, ambophilic and foamy, acidophilic and fibrillar or completely absent. The amount of matrix varies inversely with the degree of cellularity. Lichtenstein and Jaffe[8] have stressed the importance of detailed cytologic study in the diagnosis of some chondrosarcomas. We agree in general with their tenets. The cells of malignant cartilaginous tumors regardless of type contain relatively large nuclei which may be either granular, vesicular, compact or hyperchromatic. Cytoplasm is homogeneous, granular or vacuolated. Binucleate cells are present, often in large numbers. Multinucleated forms and even true tumor giant cells may be found in some chondrosarcomas. Mitotic figures are usually not present in high concentrations. Vascularity varies widely. Most of the blood vessels are contained in the pseudocapsular tissue and follow septa into the substance of the tumor. It is extraordinary how few viable blood channels may be seen in some huge chondrosarcomas while other, considerably smaller, may contain highly vascular areas. One occasionally sees endothelial lined spaces completely surrounded by neoplastic tissue. We have gained the impression that more vascular chondrosarcomas metastasize more readily than those in which vascularity is not conspicuous. This may be related to the tendency for these neoplasms to invade veins and form tumor thrombi.

Chondrosarcomas affect men more often than women. They occur relatively later in life than the more malignant osteogenic sarcomas. The mean age of the 74 cases studied was 38 years, the youngest 13, the oldest 67. It is difficult to estimate the real duration of these tumors because many of them give little evidence of their presence and some are obscured by their anatomic location. Only three of our patients had symptoms for less than a year. The average duration of symptoms in the other nine was 4.5 years but this is heavily weighted by those people with recurrent tumors. The majority of all the cases we have studied had symptoms for more than 12 months before they sought treatment. Pain or a mass are the common complaints. Pain is mild and intermittent at first but increases in intensity and becomes constant over a long period of time. The lesion is usually extensive when a patient complains of both tumor and pain. Physical examination reveals little unless a palpable mass is present. There is occasionally a sensation of increased warmth over these tumors, some even appearing inflammatory. Other findings are due to the mechanical effects of the tumor by limiting motion and impairing function.

On roentgenographic examination chondrosarcomas form poorly delimited, bulky masses. The central lesions, as Phemister noted, produced expansile swelling of the shaft which may be associated either with thickening or dissolution of the surrounding cortical bone.[11] Peripheral chondrosarcomas excavate the bone but are rarely associated with visible evidence of periosteal bone formation. The bulk of the tumor is extra-osseous. Focal areas of calcification, when present, produce small, irregular, fuzzy blotches and streaks of increased

density. Occasionally chondrosarcomas have a bony pedicle. We interpret this as presumptive evidence of pre-existing osteochondroma. Involvement of joint spaces is distinctly rare although most of these tumors arise near the ends of long bones and extend in their long axes.

Chondrosarcomas vary widely in their growth potentialities. Some remain well localized despite multiple recurrences. Others metastasize widely within a relatively short time. The difficulties encountered in estimating the prognosis of chondroid neoplasms and the effects of surgical therapy are best shown by specific examples.

The first four cases to be reported, Nos. 1 to 4 incl., had chondrosarcomas in the extremities where clean cut amputation could be performed well away from the growths. Case 4 was associated with Ollier's disease and multiple hemangiomata. Despite the multiplicity of benign chondromas only one malignant cartilaginous tumor has been found. All of these patients have remained well without recurrence for at least six years, and are undoubtedly cured.

The protracted course of some relatively indolent forms of chondrosarcoma are exemplified by the next three cases, Nos. 5, 6 and 7. The initial operation in each case was inadequate. Recurrences followed but no evidence of metastasis was ever found although the recurrences grew more rapidly and appeared more anaplastic than the original tumors.

The eighth case was a sacral chondrosarcoma inoperable from its inception. It produced peritoneal implants with fatal issue 20 months after the onset of symptoms.

With Case 9, there were three cartilaginous tumors. The one in the pelvis was malignant. It recurred after partial excision and eventually metastasized to the lungs. The histologic appearance of the chondrosarcoma was less distinctive than usual. Even the metastases lacked the usual cytologic features of chondrosarcoma. We cannot eliminate the possibility that each of the masses described represents an individual neoplasm unrelated to the others. This, however, seems improbable.

Case 10 is a more highly malignant type of chondrosarcoma than any of the previous ones. A large cartilaginous tumor containing small areas of undifferentiated pleomorphic sarcoma was excised from the ilium. Metastases developed soon afterwards.

Interinnomino-abdominal amputation would seem to offer a better chance for cure of chondrosarcomas of the pelvis than would local excision. The following cases were huge tumors removed by hind-quarter section. The results are disappointing. Cases 11 and 12 have been reported previously in more detail.[9] Cases 7 and 10 might have been salvaged by hind-quarter amputation but circumstances were such that this operation was not advised.

Not all bulky cartilaginous tumors are malignant. The last case (Case 14) was a huge chondroma arising from the tibia. It was recognized and removed locally with a successful outcome.

There are two factors responsible for our poor results. The first is improper evaluation of the malignant potentialities of some chondroid tumors; the sec-

ond, inadequate surgery. The differential diagnosis between chondroma and chondrosarcoma may be difficult.

Chondrosarcomas may appear encapsulated on macroscopic examination but we have not seen any instance in which a distinct capsule intervened between chondroid tissue and adjacent cancellous bone. On the contrary, invasion of the marrow spaces was demonstrated histologically in each case. Perhaps this accounts for the poor results following curettement or excision. One is loathe to sacrifice more bone than seems necessary and macroscopic examination fails to reveal the true extent of the lesion within bone. Our experience indicates that benign cartilaginous tumors are well circumscribed if not completely encapsulated. We have not observed invasion of the spongiosa by neoplastic cells in those chondroid lesions which responded favorably to curettement. It would seem that local recurrence in bone may be a reasonably good criterion of at least locally malignant chondrosarcoma unless strong evidence to the contrary can be adduced. When such a recurrence is noted a radical removal of the area is indicated if there is to be a cure.

There is little that can be seen on the cut surfaces of some chondroid tumors that might lead one to suspect their malignant character. Both chondrosarcomas and chondromas may be bulky. Both may be lobulated. Both may contain gelatinous, cystic or calcified areas. Chondrosarcomas, however, seem to be more destructive. Eccentrically placed chondrosarcomas reduce the affected bone to a melange of gritty and hyalin material in which the outline of the bone is seldom retained. Both central and peripheral types tend to extend in the bone's long axis.

A final determination of the status of a given chondroid lesion must rest on consideration of *all* the facts. Histologic examination is extremely important and particularly the cytologic characteristics stressed by Lichtenstein and Jaffe.[8] The pathologist's examination must be thorough. Many sections are essential. Close inspection of multiple cut surfaces sometimes reveals small fibrous-appearing areas containing tissue totally different in histologic character from the tissues comprising the more bulky part of the neoplasm.

We have found no absolute histologic or cytologic criteria which distinguish the locally invasive chondrosarcomas from those that metastasize to distant organs other than the foci of frank osteogenic sarcoma encountered in only two cases. The character of the matrix seems to be of little importance. Myxomatous tissue has no evil connotation in our experience. Bloodgood reported benign myxomas of bone that responded favorably to conservative surgical measures.[1] We have had similar experience. Certainly the more aggressive chondrosarcomas seem to be more cellular than those that remained well localized. A great variety of cell types were found among these neoplasms and in individual members of the group. No correlation of type of cartilage cell with biologic behavior seems possible. The single most constant change that characterized the group was the presence of relatively large nuclei in most of the cells. The nuclei were either granular or vesicular and attained maximum diameters at least one half that of the cells in which they lay. This contrasted

sharply with the small pyknotic nuclei commonly less than one-third the greatest cell dimension seen in most chondromas. Binucleate cells were seen in all of the chondrosarcomas. Tumor giant cells were a distinctly evil omen. Mitotic figures were found rarely among cartilage cells in the great majority of our cases.

The two patients whose metastases contained no cartilaginous elements are particularly interesting. Had tissue for histologic examination been taken only from the bulky 90 per cent of these tumors their true nature would have escaped detection. In Case 12 the significant area was obscured by cartilage that overlapped the hip joint. Even the tumor component that invaded the medulla of the femur was frankly chondroid. It is possible that some of this patient's metastases may have contained cartilage but permission for post-mortem examination could not be secured. The second patient's tumor (Case 10) contained multiple foci of highly anaplastic sarcoma imbedded in frankly cartilaginous neoplasm. No cartilage has been found in any of the metastases yet examined. There are a number of cases recorded in the Bone Sarcoma Registry in which obviously chondroid neoplasms fulfilling the modern criteria for the diagnosis of chondrosarcoma developed metastases that contained spindle cell and/or osteogenic elements but were devoid of recognizable cartilage. We believe that the prognosis among patients whose chondrosarcomas contain foci of anaplastic fibrosarcoma or histologic osteogenic sarcoma, however small, is much less favorable than in those whose tumors contain only recognizable cartilage or its precursors. One may argue that there is little difference between these two cases and the more readily apparent osteogenic sarcomas. We would point out that osteogenic sarcomas as commonly denoted are tumors affecting younger individuals. Frank osteogenic sarcoma among older people is usually associated with osteitis deformans. Another important difference is the slowly progressive character of the lesions. This is shown particularly well in Case 12 who was known to have had a cartilaginous neoplasm for at least six years. The other example is less convincing although it seems incredible that the neoplasm found at operation could have been present for only the four months indicated by the history. This tumor arose in an inaccessible location where a large mass could easily escape detection for a long time and might easily fail to produce symptoms.

There is little doubt that highly malignant chondrosarcomas may evolve from benign cartilaginous tumors.[4, 5, 8] We found no absolute proof of a pre-existing benign lesion among any of our cases yet there is good evidence of changes in the structural characteristics of individual tumors over long periods. In at least two patients multiple sections from the first tumors available for study failed to reveal unequivocal histologic evidence of chondrosarcoma. The patterns seen were identical with those found in some phalangeal chondromas which responded favorably to simple curettement. It is possible that a nidus of more anaplastic tissue escaped detection. We do not think so. The recurrences in each instance were more clearly sarcomatous than were the parent tumors. In some cases the recurrences became progressively more anaplastic

over a period of time. It should be recalled that surgery altered drastically the natural habitat of the tumor cells affecting their relationships with other tissues and particularly their blood and nerve supply and their lymphatic drainage. We would suggest that competition for survival required the development of new characteristics by the neoplastic cells which were reflected in their growth potentialities and morphologic features. Supporting evidence for this contention is found in the work of Spencer and Calnan[12] and Earle.[2] The situation seems to be exactly analogous to the well-known development of neurogenic sarcoma after repeated incomplete excisions of recurrent neurofibromas.[4] There can be little doubt that chondrosarcomas may evolve "spontaneously" from pre-existing chondromas or osteochondromas. It seems probable that inadequate surgery may contribute importantly to such a sequence of events.

Surgery is the only effective means of treatment of chondrosarcomas. Roentgen therapy may relieve pain but seems to be totally incapable of reducing appreciably the size of the mass in therapeutic dosages. We advise amputation for chondrosarcomas of the extremities. A wide zone of normal tissue must intervene between the lesion and the line of amputation if the procedure is to be successful. This may seem unnecessarily radical in those cases where the cytologic characteristics are the only findings that indicate a malignant tumor. Our decision is based on a comparison of end results of surgical treatment of tumors situated in the axial and appendicular skeletons respectively. We found that most types of chondrosarcoma arising in the pelvis recurred after currettement or wide excision whereas histologically similar neoplasms affecting the extremities were usually cured by clean-cut amputation. There is hope for patients even with large tumors of the pelvic bones or the trochanteric region of the femur but interinnomino-abdominal amputation is a formidable operation. Our poor results suggest that hind-quarter section should not be delayed until everything else has failed. Gordon-Taylor's[7] and Pack's[10] experience lends support to this opinion. For practical purposes it may be wise to excise or curette a suspicious chondroid tumor but the experience of Ghormley and Meyerding[6] does not support this. If unequivocal evidence of chondrosarcoma be present further treatment will probably be essential. We recommend that this be carried out at once in those patients whose neoplasms are poorly differentiated. The well differentiated tumors may be expected to recur locally before metastasizing. It would seem, then, that more radical procedures can be delayed safely until recurrence has confirmed the diagnosis.

CASE REPORTS

Case 1.—F. R., No. 141241, a man age 58 was admitted to Strong Memorial Hospital June 8, 1938. Six months ago he bumped the middle finger of his right hand on a barrel. It did not swell or pain much and did not prevent him from working. Two months ago the finger had a lump on the dorsum at the distal end of the proximal interphalangeal joint. The joint was stiff. There had been a gradual painless enlargement of the finger.

Examination showed a greatly enlarged middle finger with a fusiform bony and rubbery-feeling growth. This was a tumor of the basal phalanx.

Roentgenograms showed a thickened basal phalanx of the middle finger. There was

irregular overgrowth of bone at the distal end of the phalanx and a large soft part swelling with fine calcifications.

The finger was amputated and the end of the third metacarpal removed with it. Local anesthesia was used. The result was excellent.

Two weeks after amputation he returned to his work which was of a heavy manual type. He was able to use his hand without trouble. Examination on Sept 30, 1946, eight years after operation, showed a normal width of the metacarpal arch. The skin was healed, soft, and there was no evidence of tumor. Roentgenograms of the hand revealed a smoothly rounded stump of the metacarpal with no evidence of recurrence.

Pathologic Examination: A globular subcutaneous mass distended the skin of the proximal phalanx of the third finger which had been amputated with the distal 3 cm. of the third metacarpal. The mass was gray-white, rubbery and translucent on cut section, 3.5 cm. long, attaining a maximum thickness of 1.5 cm. It replaced the distal centimeter of cortical bone of the dorsal surface of the phalanx and extended proximally between the periosteum and the extensor tendon almost to the metacarpophalangeal joint.

The tumor was composed of poorly encapsulated atypical hyalin cartilage in which no lobulations were seen. The cells, grouped together to form highly cellular areas, were generally ovoid or fusiform, varied greatly in size and had homogeneous acidophilic cytoplasm and relatively large round granular nuclei with conspicuous central nucleoli (Fig. 1). Multinucleated cells were found in each high power field. Tumor giant cells were seen occasionally though mitotic figures were absent. Many thin-walled blood-vessels were present at the periphery of the tumor but the center was avascular and contained focal areas of necrosis.

Case 2.—F. S., No. X8679, a 53-year-old tailor had mild pain in the ring finger of his left hand two years before consulting his physician. One and a half years before he had noted a swelling of the finger. He finally went to his doctor because he had steady pain in the area.

The finger was amputated in 1937.

Since the operation he has had no signs or symptoms of any kind. He returned to his work as a tailor and has worked daily since then. On Sept. 27, 1946, he showed no signs of recurrence or metastasis, nine years since his operation.

Pathologic Examination: The proximal two-thirds of this fourth finger which had been amputated at the metacarpophalangeal joint was distorted by a firm subcutaneous mass. On cut section the proximal phalanx was completely replaced by a lobulated translucent mass of refractile, milky-appearing tissue which extended along the palmar surface of the middle phalanx between the periosteum and flexor tendons. The entire tumor was 8 cm. long and 4.5 cm. in greatest diameter. The center of the lesion was soft and the periphery was rubbery.

Great variation in size and shape of cells characterized the atypical cartilage that formed this tumor. Most of the cells were stellate or spindle-shaped with pale cytoplasm and relatively huge hyperchromatic nuclei. Binucleate forms were moderately plentiful but multinucleated and tumor giant cells were not found. There were no mitotic figures. The thin basophilic matrix was foamy and pale. Lobules were poorly defined. The tumor was surrounded by highly vascular cellular areolar connective tissue infiltrated with lymphocytes. Tiny spicules of bone were seen near the periphery of the mass.

Case 3.—No. 161676. L. L., married female, age 55, was admitted to the Strong Memorial Hospital, Feb. 11, 1940. She had had mild progressive pain for one and a half years on the inner aspect of the left foot. An enlarging tumor was noted eight months ago. She had been treated for flat feet by strapping and arch supports without relief. Two weeks ago for the first time she had x-ray pictures taken. Following a biopsy she was referred to the hospital for further treatment.

Her family and past histories had no bearing on the present complaint.

Examination showed an obese healthy looking woman. She weighed 220 lbs. Her

vital signs were normal. She had a ventral hernia in an abdominal scar. Her left foot showed a swelling on the medial aspect at the proximal end of the first metatarsal bone. The mass was smooth, firm, not movable, and measured 5 x 7 cm. It was tender and there was edema of the tissues of the dorsum of the foot in this region. There was a limitation of subastragular motion by approximately 70 per cent.

Laboratory studies showed red blood cells 4,940,000, hemoglobin 14.5 Gm., white blood cells 9,600. The Wassermann reaction was negative. Roentgenograms revealed marked decalcification in all the bones of the foot. The cortical bone on the medial side of the cuneiform was partially destroyed. There was a soft tissue mass in the same area.

A mid-calf amputation was done on Feb. 13, 1940. She was discharged with a soft, well healed, non-tender stump on March 10, 1940.

She had an artificial limb fitted. This worked well till Feb. 3, 1943, when it had to be refitted. There were no signs of recurrence or metastasis at that time.

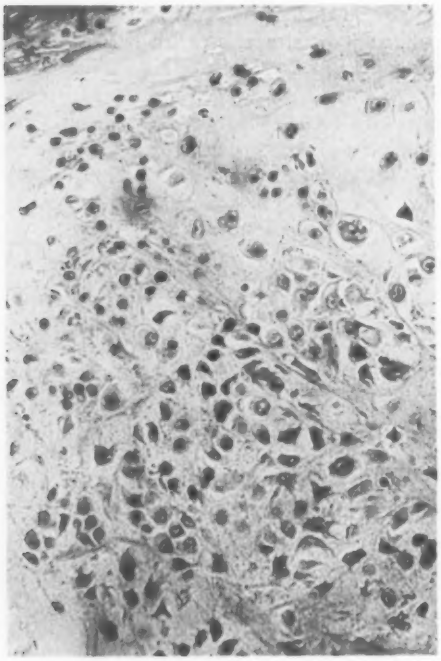

FIG. 1

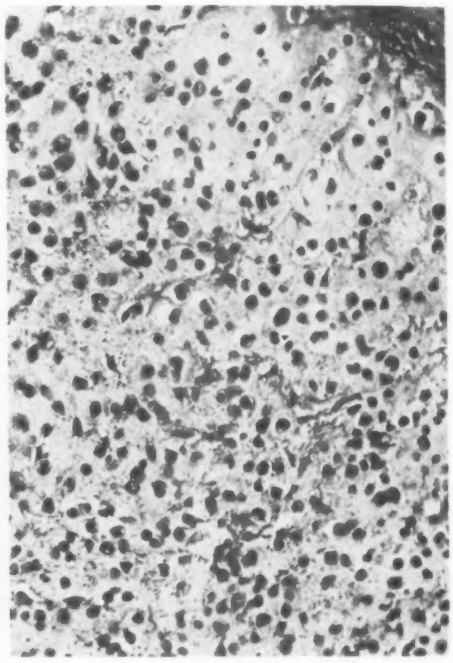

FIG. 2

FIG. 1.—(Case 1) Chondrosarcoma of finger. (x 200)
FIG. 2.—(Case 3) Chondrosarcoma of cuneiform bone. (x 200)

On Dec. 30, 1946, she was working daily and had no complaints, 6¾ years since operation.

Pathologic Examination. A rubbery globular mass 8 cm. in diameter and 7 cm. thick protruded from the medial aspect of the first cuneiform bone overlapping the head of the first metatarsal and the navicular. On cut section the first cuneiform was almost completely replaced by soft, glistening, translucent, gray tissue continuous with the tumor extending from its medial aspect. The medial surface of the mass was covered by tough fibrous tissue but the intra-osseous part of the lesion was not encapsulated. The tumor did not encroach on the joint surfaces.

The cellular neoplasm was composed of atypical hyalin cartilage (Fig. 2). The cells were round or ovoid and varied widely in size. The nuclei were relatively large, granular

and had prominent nucleoli. Hyperchromatism was moderate. The cytoplasm was granular and acidophilic. Multinucleated cells were found in most fields but there were no tumor giant cells or mitotic figures. The matrix was generally hyalin and basophilic but some areas were foamy and stained palely. Well formed spicules of bone were seen near the edge of the tumor and its medial surface was covered by avascular collagenous tissue infiltrated with lymphocytes and plasma cells. Fibrous septa traversed the neoplasm.

Case 4.—V. F., No. 780, a 33-year-old man was admitted to Strong Memorial Hospital Dec. 4, 1934.

He has had a long history of multiple fractures dating from infancy. There have been five fractures of the left femur; two of the left tibia and one of the left forearm. As a result of one femur fracture he has had a deformity of the left thigh since eight years of age. Since birth there has been bilateral dislocation of the elbows and small, hard, irregular tumors on the digits of the left hand. Soft bluish discolorations have been present on the left foot, lower leg, about the knees, left hand and forearm. In March, 1924, he had hemoptysis. He was put at bed rest for nine months. Tubercle bacilli were never demonstrated. He gained from 98 to 115 lbs. during this time. There has been a right-sided nodular goitre for 11 years. For one year he has had intermittent pain in the left ankle. This pain has become steadily worse. The only relief is obtained by strapping with adhesive. He has walked with crutches since childhood and the left leg is eight inches shorter than the right. He has had occasional spells of dyspnoea, palpitation and tachycardia.

His father died at 62 of heart disease, his mother died at 69 of cancer of the rectum. One sister died at 11 of "heart trouble" and one sister died at 35 of "some blood stream disease." Two sisters are living and well. There has been no family history of bone fragility or bony deformities.

Examination revealed multiple deformities. There was an acne-like rash over the face, back and buttocks. The sclerae were not blue. There was an enlarged nodular goitre on the right. The heart and lungs were normal. The blood pressure was 120 systolic, 68 diastolic. The shoulder girdle, spine and pelvis appeared to be normal. The left humerus was shorter than the right with an old fracture deformity. Both radii were dislocated at the elbows. Both forearms were bowed and malformed, the left more so than the right. The left ulna showed an old fracture deformity. The fingers of the left hand have multiple chondromata as also the left toes and foot. There were many small cavernous hemangiomata on the left hand and forearm. The right leg was normal. The left leg was shorter than the right, with fracture deformity of the left femur, upper third. There was some limitation of the left hip with muscle atrophy.

Laboratory Examinations showed normal blood, urine and negative blood Wassermann. The blood calcium was 10.0 mgs. per cent and the phosphorus 3.4 mgs. per cent. Roentgenograms showed the characteristic picture of multiple cartilaginous exostoses with malformations of the bones characteristic of the disease.

He was advised to have the left leg amputated at the midthigh because it did not take part in weight bearing, was painful and a good artificial limb would allow him to discard his crutches. Amputation through the mid thigh was done under spinal anesthesia. Convalescence was without incident. He was discharged on Dec. 22, 1934, in good condition. He was fitted to an artificial limb and managed it quite well. He worked hard at his concession putting in long hours daily.

Report on Dec. 24, 1946, from Chicago, Ill., where he is now living was that he "is feeling fine and working daily." This is 12 years since operation.

Pathologic Examination. The leg bones were bowed anteriorly and laterally. The skin was studded with hemangiomata, some of them pedunculated. Other hemangiomata were found in the subcutaneous tissues of the leg and foot. The bones were studded with irregular masses of typical hyalin cartilage. The second toe was almost replaced by a friable cartilaginous mass.

The lesion of the toe contained areas of atypical hyalin cartilage and others that were frankly myxomatous. These types of tissue were sometimes mixed together. The cells in the hyalin areas were moderately numerous, ovoid with relatively large granular nuclei which became hyperchromatic at the periphery of these areas. Stellate cells of the myxomatoid zones had rather small compact nuclei. Binucleate forms were found in each high power field but no tumor giant cells nor mitotic figures were recognized. The tumor was only partly encapsulated since masses of neoplastic cells were found adjacent to relatively normal appearing bone. Septa were rudimentary and vascular. Endothelial lined spaces filled with blood were found imbedded in tumor cartilage.

Case 5.—No. 150027, I. L., married female, age 33, was admitted to the Strong Memorial Hospital, Feb. 13, 1939. She first became aware of a hard tumor on a rib just below her left breast in April, 1933. There were no accompanying symptoms. Her physician advised watching the tumor, which was about the size of a red kidney bean. One year later it had increased to the size of a lemon. It was removed with a piece of the rib—"about four inches long" according to the patient. Convalescence was uneventful. Fifteen months later a small nodule appeared in the scar at the site of the first tumor and a second soft, non-tender, fast growing, movable, fluctuant area at the end of the scar. By the spring of 1937 she began to have aching and tenderness in the tumor. In the summer of 1937, seven irradiation treatments were given at the State Malignant Disease Institute. Tenderness and soreness increased locally following this. In October 1938 a mass was removed at a hospital in Syracuse, N. Y.

Her family and her past histories did not contribute to her present condition.

She was a well nourished, handsome young woman. Her vital signs were normal. There was a scar on the left chest from the xiphoid along the 7th rib to the axillary line. A moderately tender mass, measuring 5 x 10 cms. was present extending over the 7th, 8th and 9th ribs in the midclavicular line. There were two other movable masses of 1 x 2 cm. and 1 x 1 cm. noted in the anterior axillary line. The lungs were normal to physical examination. The rest of the physical examination did not reveal anything significant.

Laboratory Studies showed red blood cells 4,200,000, hemoglobin 13.5 Gm., white blood cells 6,000. Wassermann reaction was negative.

Roentgenograms indicated that there were no metastases in the lung fields. The tumor involved the 7th, 8th, and 9th ribs and cast a sharply defined ovoid shadow with a network of calcification within the mass.

On Feb. 16, 1939, a resection of the 7th, 8th and 9th ribs was done in one block with all the intervening tissues and including the separate nodules. A good margin was given and great care taken not to expose any of the tumor. It was evident at operation that the tumor had broken through its original capsule. It had extended by direct continuity along the fascial planes and across the pleura on the inside of the chest. The diaphragm and the lung gave no evidence of involvement.

She made a good recovery and was discharged to her home on March 8, 1939.

She was completely symptom free and gained in weight until July 25, 1939. Then she had pain starting in the mid-dorsal spine and radiating around the chest wall along the scar. Pain was accentuated by motion, standing, fatigue, and relieved by recumbency. The pain had become persistent and severe so that she had been given "pain pills" for relief.

On examination she showed tenderness over the 6th dorsal vertebra and moderate sensitiveness in the scar. There were no evidences of recurrence at the site of operation. Nothing else of importance was found. Studies on the blood were almost identical with those of her first admission.

Roentgenograms showed malignant invasion with destruction of the left pedicle of D6, both pedicles of D7 and a partial involvement of the posterior aspects of the bodies of both D6 and D7. There was moderate deformity of the paravertebral structures. Radiation treatment with x-rays was given consisting in 2000 "r" units in 10 days. She was

placed on bed boards and at complete bed rest. Relief from the pain was quite marked as long as she was recumbent. Upon getting up pain returned with lessened severity. She was discharged on Oct. 21, 1939.

In late December, 1939, her right leg became weak and slightly numb. In another month both right and left legs had become completely paralyzed with loss of all sensation. There was also incontinence of urine and feces. On this admission there was a kyphosis at D7–8 and 9; complete loss of sensation below D8; a small nodule on the left third rib in the mid-clavicular line; and a freely movable lemon-sized mass above and lateral to her right breast. Her hemoglobin was now 12.2 Gm. Stereo examination of the spine indicated marked destruction of the bodies of the 6th and 7th dorsal vertebrae and involvement of the rib ends. There was also invasion of the 11th rib and the 11th dorsal vertebra. Gallstones were present. She responded well to aspirin and codeine therapy. She was put on constant bladder drainage. She was discharged to her home on June 29, 1940, where she died during the summer.

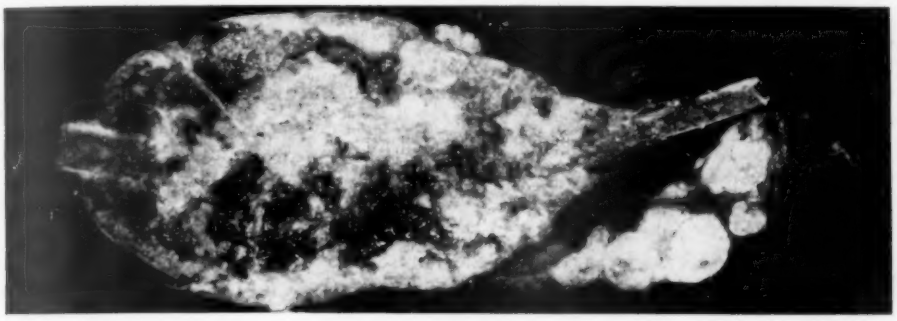

FIG. 3.—(Case 5) Recurrent chondrosarcoma of rib.

Pathologic Examination.—The specimen, weighing 250 Gm., consisted of segments of three ribs, each 14 cm. long. The central rib was obscured by a resilient circumscribed ovoid mass measuring 9.5 x 6.5 x 6 cm. which covered the central part of the adjacent ribs and distorted the pleural and muscular surfaces of the specimen. Mucoid material oozed from the gray translucent lobulated cut surfaces leaving scattered craters lined with ragged tissue. The central rib was entirely destroyed within the tumor and the adjacent ribs were eroded. A tongue of nodular tumor tissue extended dorsad along the outer border of the central rib invading the intercostal muscles. A rim of normal appearing bone and muscle at least 1 cm. wide separated the tumor from the dorsal edge of the specimen (Fig. 3).

The cartilage in this neoplasm was atypical and highly cellular. There were ovoid cells with relatively large vesicular nuclei and spindle-shaped and stellate cells with relatively small hyperchromatic nuclei. These types were present in approximately equal concentrations. Cytoplasm was scanty. Binucleate forms were commonly found but no tumor giant cells or mitotic figures were seen. The matrix was pale and vacuolated and was absent in the areas where the stellate and fusiform cells predominated. The tumor was confined by a thin rim of poorly vascular collagenous tissue.

The nodules noted in the intercostal muscles possessed the same cytologic characteristics as the parent tumor. They were circumscribed but not encapsulated.

Case 6.—M. F., No. 104576, a 54-year-old housewife, was admitted to Strong Memorial Hospital on July 15, 1935.

She suffered a severe fall injuring her right thigh and knee eight years ago. While on ship board three years ago she had another fall. One year ago she noticed difficulty in getting up and down stairs. She began to have stabbing pains radiating around her left chest from the spine to the lower portion of the sternum three months ago. For several weeks while this pain persisted there was an extremely sensitive zone in the involved skin area. For the first time one month ago she had numbness of her feet. This numbness has gradually progressed upward with a sense of weakness at the same time. She has had to use crutches to get around.

Her family and past histories were non-contributory.

Examination gave tenderness on pressure over Th 3, 4, and 5. There were hyperactive biceps and triceps reflexes on the left; and a bilateral positive Babinski. Sensory changes to pin prick, touch, hot and cold at Th 6. Vibratory sense was lost below level of ischial spines.

Laboratory studies showed normal blood and urine. Wassermann on the blood was negative. Radiograms showed a destructive erosion of the pedicles of Th 4 compatible with tumor growth.

Laminectomy was done. A hard, round, circumscribed nodular tumor was encountered. It measured 3.5 x 4.0 cm. in diameter. There were two portions of the growth, one involving the muscles of the back and the other an intraspinal extension. All the tumor was looped out except for a thin shell which was left between the 4th and 5th ribs on the pleura.

The postoperative course was uncomplicated. The positive Babinski bilateral signs disappeared. She had almost complete restoration of the power of her lower extremities. She was discharged on Aug. 5, 1935.

She was readmitted on July 28, 1936. She had regained full use of her legs and her only complaint was crampy pains over the left scapula. These pains first appeared in Mar. 1936 and had gradually increased in severity, causing her to cry out. There had been sweating of the right side of the face, right arm and axilla for the past three weeks.

On examination the only significant finding was that the right knee jerk was a little more active than the left.

Laminectomy with partial excision of the tumor was carried out. The tumor had extended into the thoracic cavity.

She was discharged in good condition on Aug. 18, 1936.

Her third admission was on June 8, 1937. At this time she had difficulty in walking and pain in the right hip. She had a band of anesthesia corresponding to T3 and T4 (two roots sectioned at last operation). The right leg was weaker than the left. Roentgenograms showed traumatic arthritis right hip—old (injury).

Her fourth admission was on Jan. 3, 1938, because of inability to walk. This complaint had been present one week. There was discomfort, weakness and pain in the right shoulder and in both thighs. There was anesthesia to pin prick, touch and temperature to Th 2. The old incision was opened and access to the intrathoracic portion of the tumor was obtained by removal of portions of 3rd, 4th and 5th ribs. Tumor tissue was resected as completely as possible. She made a beautiful recovery with return of sensation to practically normal. A course of deep roentgenotherapy was given.

She died at her home in the summer of 1939. No postmortem study was made.

Pathologic Examination: The three surgical specimens appeared similar. They were moderately small pieces of cartilaginous tissue varying in consistency from soft to firm.

The original neoplasm was made up of atypical adult type hyalin cartilage in which groups of small ovoid cells were separated by homogeneous basophilic ground substance. The cells had acidophilic cytoplasm and relatively large granular nuclei. Multinucleated forms were seen in each high power field but there were no tumor giant cells nor mitotic figures. Some areas were necrotic. A moderately vascular capsule was seen in some areas

but tumor cells filled the marrow spaces of adjacent bone. Septa were poorly defined (Fig. 4).

The first recurrence was more cellular. Nuclear hyperchromatism was conspicuous. Some bizarre nuclei were seen. The entire lesion was more vascular than the original tumor (Fig. 5).

The second recurrence was more anaplastic although still recognizable as chondroid tissue. The hyalin matrix contained acidophilic fibrils. Tumor cells were larger and giant forms were found easily but only a few mitotic figures could be seen. The periphery of the neoplasm was very vascular (Fig. 6).

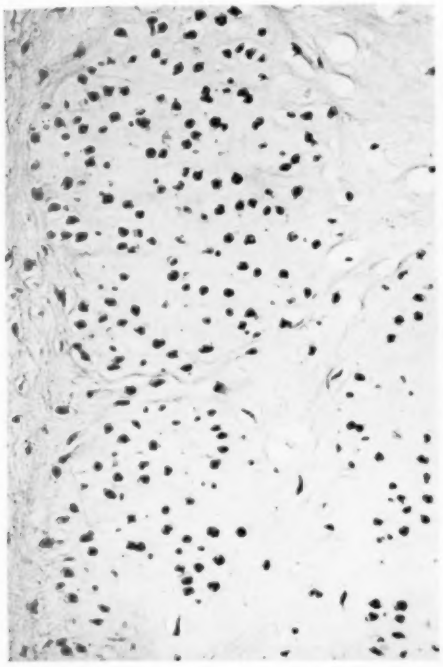

FIG. 4

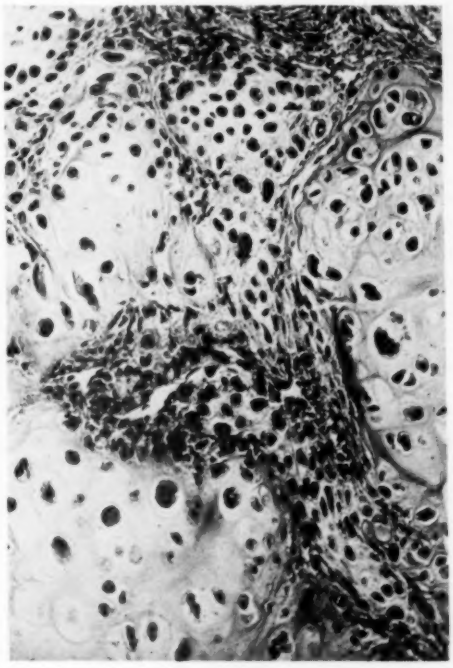

FIG. 5

FIG. 4.—(Case 6) Chondrosarcoma of spine. Photomicrograph of original tumor. (x 200)

FIG. 5.—(Case 6) Recurrent chondrosarcoma of spine. The tumor is more poorly differentiated than the original neoplasm excised one year previously. (x 200)

Case 7.—Hosp. No. 90595, H. A., single female, social service worker, age 40, was admitted to the Strong Memorial Hospital, June 22, 1934. While looking in a mirror three months previously she had noticed that the left hip was more prominent than the right. On examining the hip she had found a tumor. Two months ago she had had pain down the lateral and posterior surfaces of the left leg as far as the ankle. This pain was worse when she worked hard or got tired. It was worse at night and had persisted till the time of admission. There had been tenderness over the swelling recently but no motor weakness. She had been dieting and had lost 18 pounds.

In June, 1933, she had a sudden attack of blindness in the left eye. She went to an ophthalmologist who diagnosed a thrombosis of the central artery of the retina. Under his treatment she had recovered part of her vision in the lower half of the field but the upper half remained blind.

She had had bilateral slipping patellas since childhood. One side had been dislocated 13 times; the other 14 or 15 times. Her father, a physician, had always reduced the dislocations without difficulty. There had been no slipping in the last 10 years.

She was well developed and obese, comfortable and cooperative. There were many pin-head to bean-sized rusty areas of keratosis over the trunk. The vision was normal in the right but only 20/200 in the left eye. The left pupil was slightly larger than the right. The left fundus showed secondary optic atrophy with marked reduction in the calibre of the retinal arteries. There was a huge swelling in the left gluteal region extending as low as the gluteal fold. It distorted the whole gluteal area. The tumor extended almost to the midline of the abdomen, above the iliac crest and down to the level of the left greater trochanter. It was deep under the muscles, was firm, semi-elastic. There were a few dilated vessels in the skin over it and a sensation of increased warmth. No nodes were palpable in the groin. Rectal examination gave no evidence of extension into the pelvis. The tumor area measured 15.0 cm. x 8.0 cm. x 8.0 cm. There was no limitation of motion in the femur.

Laboratory Studies showed red blood cells 5,600,000; hemoglobin 13 Gm.; white blood cells 6,400. Wassermann on the blood was negative. Roentgenograms of the chest were negative for metastases. Roentgenograms of the left pelvis showed multiple patches of partial calcification scattered over the region of the buttocks. There were three distinct punched out areas through the upper portion of the ilium as if invasion had taken place. The roentgenographic picture was typical for chondrosarcoma of the ilium.

The consensus was that operation could not be done and although this type of tumor was known to be radioresistant, a course of radiation therapy was decided upon. During the next six months she received x-radiation therapy in 300 r. doses for a total of 13,500 r. There was no appreciable effect upon the tumor. Accordingly on Jan. 3, 1935, the tumor was exposed and found to spring from a 10 cm. wide base near the upper crest of the ilium. This pedicle was divided with a chisel and the main portion of the tumor thus removed. The area of the pedicle was next chiseled out with a good margin, making a hole through the bone. Several small fragments of cartilage were broken off during the operation and the wound was thoroughly washed out at the close. The gluteus muscles were preserved carefully. Silk was used throughout. The operation took three hours. There was no shock. A transfusion of 400 cc. of citrated blood was given late in the day. The wound healed by first intention. She was discharged on the 11th postoperative day. She recovered rapidly, walked without a limp and resumed her job as a visiting social service worker a month after operation. Roentgenograms showed a hole through the ilium and no signs of remaining tumor in the bone.

Six months later (June 19, 1936) a good sized nodule was found in the scar. It was removed without ever exposing any of it.

Her next recurrence was discovered on Oct. 29, 1937. It was excised with the radio-knife without any difficulty.

In Nov. of 1938 she began to get sciatic pain along the back of the left thigh. She walked with more of a limp. No signs of recurrence could be found on examination. By Jan. 1940 it became apparent that she had another tumor. On Mar. 11, 1940, the tumor was again excised. It arose from inside the ilium and had extended through the opening made in this bone. It was very difficult to dislodge and finally in order to control bleeding from the sciatic artery, it was necessary to remove it rapidly in pieces. The tumor consisted of firm cartilage. It weighed 1270 Gm. and measured 18.0 x 15.0 x 10.0 cm. Serosanguinous fluid collected in the dead space necessitating aspiration. She went home in good condition on the 12th postoperative day.

In Dec. of 1940 she presented two recurrences—one the size of a hen's egg—the other, the size of a ripe olive. These tumors were easily removed. They measured 7.0 x 5.0 x 4.0 cm., and 2.0 x 2.0 x 4.0 cm. respectively. She was in the hospital for 11 days. She continued to have sacro-iliac and sciatic tenderness and numbness in the great toe. Local injections with 1 per cent procaine and epidural injections of 0.5 per cent procaine

produced temporary relief. Physiotherapy was of some help but the pain became so persistent that a chordotomy was performed at the level of D4–5– and 6. She was completely relieved of her pain by this procedure and was discharged on June 22, 1941.

Her next admission was in July 1941. A large trilobed tumor with an intrapelvic extension and two posterior ones was removed. The sciatic nerve had been compressed to a thin area by the pelvic portion of the tumor. The tumor measured 10.0 x 10.0 cm., weighed 500 Gm. It was cystic in the interior containing a thick tapioca-like gelatinous material. She was discharged on the 16th day after operation. There was a foot drop and flail-like ankle. A foot drop brace was necessary to stabilize her walking.

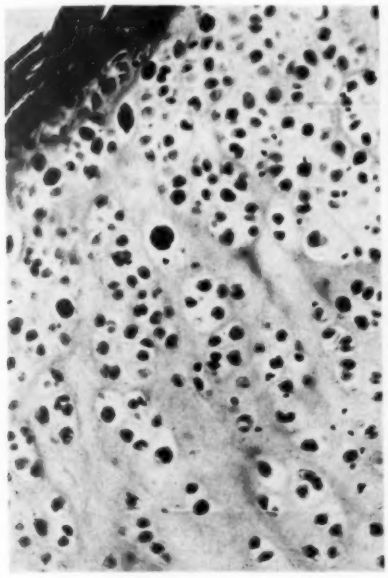

FIG. 6

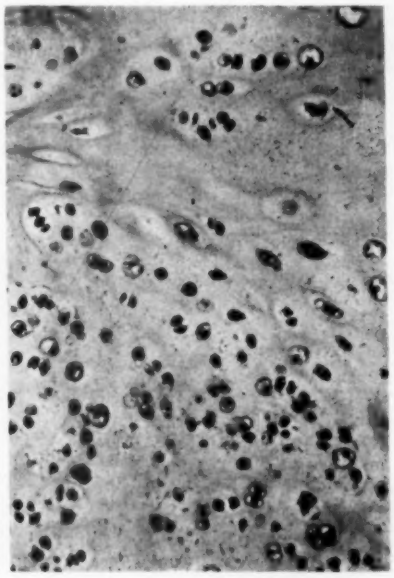

FIG. 7

FIG. 6.—(Case 6) Second recurrence of chondrosarcoma of spine Case 6 more anaplastic than previously excised specimens. (x 200)

FIG. 7.—(Case 7) Chondrosarcoma of ilium. Photomicrograph of original tumor. (x 200)

It was necessary to aspirate fluid from the dead space left by operation. This was done about once a month for the next three months. She worked daily making up to 10 calls on some days. In late October 1941 culture of this fluid showed non-hemolytic streptococci and *S. albus*. The area was incised and drained. Gramicidin was introduced into the abscess cavity. It healed in about one month but in Mar. 1942 the tumor had extended through the scar ulcerating the epithelium over it. Consequently on Apr. 2, 1942, this nodule was excised and she went home two days later. She continued with her work coming to the office for dressings. The wound was infected with *Staphylococcus aureus* and *B. proteus*. It had a disagreeable odor which was cleared by treatment with azochloramide in triacetin oil. Dressings were done every two or three days with slow healing but tumor tissue began to appear again. Accordingly the whole area was curetted out under sodium pentothal anesthesia on June 12, 1942. Gramicidin was introduced into the cavity and alternated with acetic acid 0.5 per cent as *B. pyocyaneus* infection as well as *B. proteus*

was present. The situation appeared to be very bad but healthy granulations formed and pinch grafts were applied to them. She was discharged on July 26th. For the remainder of the year she continued with her work although the wound required much attention. She also developed lack of bladder control and frequency. She also had progressive constipation. It was found that she had loss of vesical and anal sphincter tone on a neurological basis. She had acute pyelitis and cystitis due to B. coli. Sulphadiazine brought the temperature to normal and gave relief to her bladder symptoms.

On Mar. 7, 1943, she was admitted to the hospital for the last time. She had had six weeks of gradually progressive intestinal obstruction. Her bowel movements had decreased

FIG. 8.—(Case 7) Macroscopic appearance of typical recurrent chondrosarcoma.

to two times a week. She had had loss of appetite, nausea and vomiting increasing in frequency. The tumor had grown rapidly in size. She had lost weight. Everyone was much impressed by her courage in facing her problem. There was a firm irregular mass in the L.L.Q. inguinal area. There were huge firm fixed nodules over the left hip and iliac area. Her course was progressively downhill. She had a chill with cyanosis and dyspnea on Mar. 12th, possibly a lung metastasis. On the 17th her left leg became tremendously swollen and edematous. She became moribund on the 19th and expired quietly on March. 22, 1943.

Pathologic Examination.—The globular, coarsely nodular, firm, original specimen weighed 1,415 Gm. and measured 19 x 13 x 11 cm. It was enclosed in a tough fibrous capsule which was continuous with the periosteum of the bony pedicle by which the lesion was attached to the ilium. The cut surfaces were made up of a mosaic of firm, translucent, gray hyalin cartilage, softer areas of gelatinous consistency and stony hard foci of yellow-white gritty material. Well formed fibrous septa traversed the mass. The base of the tumor was sharply delimited from the bony pedicle but the adjacent bone appeared eburneous.

Histologically the neoplasm was composed of atypical hyalin cartilage which was well encapsulated and lobulated but poorly vascular. All of the cells were ovoid, lay in lacunae, and had well defined acidophilic cytoplasm with small compact nuclei. Sections taken from the periphery of the tumor were more cellular and the nuclei were relatively much larger. Binucleate forms were found only in these regions. Spotty areas of calcification were found throughout the mass (Fig. 7).

All of the recurrences appeared similar on macroscopic examination. They were generally spherical or ovoid and rubbery. All were encapsulated and on cut section mucoid material filled with irregular masses of soft cartilage escaped from the centers. This gave the lesions the appearance of thick-walled cysts with extremely ragged linings. The walls were translucent, gray-white and firm (Fig. 8).

Each of the first four recurrences had a similar histologic pattern resembling, in general, the peripheral part of the parent tumor. The cartilage, though distinctly hyalin in type, was moderately cellular. The cells were ovoid, small and possessed relatively large nuclei. Their cytoplasm was coarsely granular. Lobulations were indistinct and the rudimentary septa were highly vascular.

The fifth recurrence was different from any of the previous material examined from this patient. It was far less cellular but the cells had relatively huge nuclei. Many cells were round and had several nuclei arranged peripherally in the cytoplasm forming crescentic structures.

The sixth recurrence resembled the original tumor.

There was no difficulty in recognizing the tissue from the seventh recurrence as cartilage but it was the most anaplastic of all the specimens. The round cells varied widely in size. Their nuclei were relatively enormous and cytoplasm was granular in small cells, vacuolated in the larger ones. Multinucleated forms were plentiful. The matrix was hyalin in some areas, foamy in others but lacunae were generally well defined. The few fibrous septa that penetrated the mass were extremely vascular and some endothelial lined spaces filled with blood were found imbedded in cartilage (Fig. 9).

The specimen obtained at postmortem examination contained all of the types of tumor described above excepting that of the seventh recurrence. The capsule was deficient. Tumor cells infiltrated the surrounding tissues. Binucleate cells were commonly seen and most nuclei were relatively large. No metastases were found.

Case 8.—C. C., No. 2707, a 21-year-old girl was admitted to the Strong Memorial Hospital Sept. 4, 1926.

She was suffering with severe sacroiliac pain, urinary incontinence, extreme constipation and vomiting. She had had a sudden attack of severe pain in the left sacroiliac region 20 months ago. She was in bed for one month before the pain left. A swelling in the sacral region with some tenderness was discovered and there was "black and blue" skin discoloration of the perineum at this same time. Early in the attack she had loose watery stools but within a short time constipation was the rule. She had passed mucus and blood in the stools. She returned to her work after one month and worked until 13 months ago. Then the attack was repeated. After five days an exploratory operation was done and an inoperable sarcoma was found. She had to be catheterized four times while in the hospital. Eight months ago pain recurred again and the swelling became more pronounced. She was given a course of roentgen ray therapy. Pain disappeared for three months but upon its return another operation of some sort was done. The pain increased in severity requiring morphine for relief. Loss of appetite and vomiting became the rule. She dropped 16 pounds in weight.

Her family history had no bearing on this condition and she had always been healthy herself until this illness.

Examination revealed an emaciated girl, sallow in complexion and in much pain. The abdomen showed a prominent bulging on the right from the umbilicus to the pubis. A

tumor was readily palpable, arising from a hard firmly-fixed posterior growth. Two scars of previous operations were present in the midline. The vulva were gaping and the perineum bulging from the pressure of a hard firmly attached smooth tumor which filled most of the pelvis. She was totally incontinent of urine. A mass could be palpated by rectum. There was a visible tender swelling over the right sacrum.

Laboratory studies gave RBC. 5,110,000; hemoglobin 80 per cent, W. B. C. 5,000. Wassermann on the blood negative. Roentgenograms showed a tumor mass completely obliterating the lower part of the sacrum. There were strands of calcification in part of the tumor.

Because of intestinal obstruction a colostomy was done on Sept. 11, 1926. This relieved her obstructive symptoms and the bowel functioned well through the artificial opening for two months until she succumbed.

Pathologic Examination.—Tissue removed from the pelvic mass at operation was made up of partly encapsulated, avascular, poorly formed chondroid tissue. The cells varied widely in size and shape with blunt spindle and ovoid cells predominating. The large granular nuclei had prominent nucleoli. The matrix was foamy, basophilic, mucoid material.. No lacunae were present. Tumor giant cells and mitotic figures were not found.

At postmortem examination a tumor mass at least 20 cm. in greatest dimension projected from the ventral surface of the sacrum, which was almost completely destroyed. The mass extended into the recto-vaginal septum, through both sacro-sciatic notches and destroyed both sacro-iliac joints and the adjacent portions of the ilia. On cut section the mass contained many cysts filled with a mixture of gelatinous material and friable pink gray tissue which made up the bulk of solid material in the neoplasm. The estimated weight of the tumor was 2,500 Gm. Metastases were found in the superior ramus of the left pubis and implants of polypoid, cystic tumor nodules were seen throughout the peritoneal cavity. The tumor produced bilateral hydroureter and hydronephrosis and obstructed the sigmoid colon.

Sections from the tumor and its metastases appeared identical with those examined from the surgical specimen (Fig. 10).

Case 9.—No. 137039, L. L., single female, age 60, was admitted to the Strong Memorial Hospital, Nov. 21, 1937. On Mar. 18, 1927 a tumor of the right chest wall was removed in Ogdensburg, N. Y. Portions of the 3rd and 4th ribs were taken with the hard nodular tumor which was reported from the Bender Albany laboratory as benign chondroma. She had had it about five years before operation. There had been no recurrence. Three years ago (1934) she discovered a small swelling in the right lumbar region. It gave no symptoms till one year later. For the last two years there had been a stinging and burning sensation in this region especially when she became tired. Two months ago the discomfort increased in severity and there was radiation down the anterior aspect of the right thigh. The swelling grew rapidly in size. Medication was necessary to relieve pain and to permit sleep.

She had an injury to her back five years ago. It caused soreness for several days but there had been no subsequent symptoms. For 2–3 years there had been attacks of dizziness, coming on suddenly and lasting several days.

She was a well developed, well nourished woman with arteriosclerotic vessels. There was an operative scar under the right breast with a defect in the bony cage due to removal of the 3rd and 4th ribs. In the right lower back was a large firm mass occupying the position of the posterior right ilium. It extended as far up as the rib cage on the right and as far over as the sacro-iliac joint which was partially obscured by it. It had a bony firmness. There were many dilated skin vessels over it and a locally increased temperature. There was no pulsation in the tumor. Movements of the lumbar spine were definitely restricted. The mass measured 10 x 15 cms. in diameter.

Laboratory studies showed red blood cells 4,160,000, hemoglobin 12.5 Gm., white blood cells 6,300. Her blood pressure was 145 systolic/90 diastolic. There were 15–20

white blood cells and 1–2 red blood cells per high power field in the urine. Blood calcium was 9.4 mgs. per cent, blood phosphorus 4.2 mgs. per cent, serum alblumin 3.16 Gm. per cent, serum globulin 2.0 Gm. per cent. Roentgenograms showed a massive bone tumor of the right ilium which replaced all the normal bone adjacent to the right sacro-iliac joint. The bone had a cystic appearance with ill defined septa, typical of chondrosarcoma.

A partial resection of this large tumor was carried out on Dec. 7, 1937. It was impossible to remove the portion which extended across the region of the sacro-iliac joint. Tumor tissue was curetted away to bare bone wherever feasible. There was considerable loss of blood. The wound became infected with S. aureus and for one week she ran a fever. Roentgenograms of the chest showed a resected area of the 3rd and 4th anterior ribs and a metastatic nodule 4 cms. in diameter near the right costophrenic angle. She was discharged feeling quite well with relief of pain 30 days after operation. The wound was still draining somewhat.

The nodule in the lung field was considered a long standing one as it showed a large size and dense structure.

Following operation she gained in weight and strength. She had little trouble in getting around. Only occasionally did she have a twinge in her thigh. She was seen in Oct. 1939, had been to the World's Fair in New York without any difficulties. She came for check up as she was having dizzy spells and some return of the pain in her right sciatic distribution. Her brother, a physician who referred her here, had died of coronary heart disease five months before, leaving her without family connections. She feared that she would become a chronic invalid and was tense and apprehensive. On this examination she showed an increasing hypertension with blood pressure of 180/96—a slightly enlarged heart. Films of the chest showed a slight increase in the size of the lesion—it now measured 5 cms. as compared to 4.2 cms. in 1937. There was a local recurrence in the pelvis but it appeared that the partial removal of the tumor had been worthwhile.

She came into the hospital for the third time on June 26, 1940, because of pain in the right hip. This pain was worse in walking. It radiated down to the calf. Examination showed some extension of the bony tumor lateralwards but not marked. Her hypertensive symptoms were uncontrolled. She still had dizzy spells and nausea. A course of radiation 1,400 r. units gave only partial relief from her pain.

At her fourth admission on January 9, 1941, she stated that she had had considerable relief from her x-ray therapy of six months ago. Also, the hypertension symptoms had been much improved. There was a hard mass in the right ilium—15 cms. in diameter. The red blood count was 4,730,000, hemoglobin 15 Gm. and white blood count 5,600. Roentgenograms showed no change in the bone tumor but a slight increase in the metastatic tumor in the right lower lung field. It now measured 6 cms. across. Radiation treatment with 2,100 r. units gave some but not complete relief.

Her fifth and last admission was for severe pain in the epigastrium with radiation to the back between the scapulae. It had begun three days previously. There was nausea but no vomiting and bowel movements had been regular. The pain shifted to the paraumbilical region especially to the right. Her temperature was 38.5°, pulse 96. Respirations 24, blood pressure 190 systolic/85 diastolic. There was marked generalized abdominal spasm and tenderness over the region of the gallbladder. The white blood count was 12,000. She was watched and showed improvement, the tenderness subsiding in three days. There had been persistent distention despite treatment. Paracentesis showed no fluid. Roentgenograms revealed a distention of the small bowel consistent with obstruction. At operation under pentothal sodium and local procaine the gallbladder was normal. A left ovarian cyst was impacted in the pelvis, trapping the small intestine. The cyst was easily removed freeing the bowel. Closure was made with silk. Although the operation was simple and practically without blood loss, the blood pressure dropped rapidly during operation following administration of the sodium pentothal. She was given plasma with a restoration of her pressure to normal. But during the night her condition became worse. Her temperature rose to 41°, the pulse was rapid and weak. The next day her fever

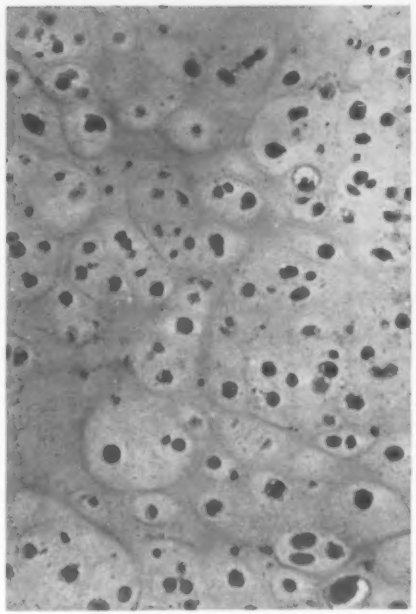

FIG. 9

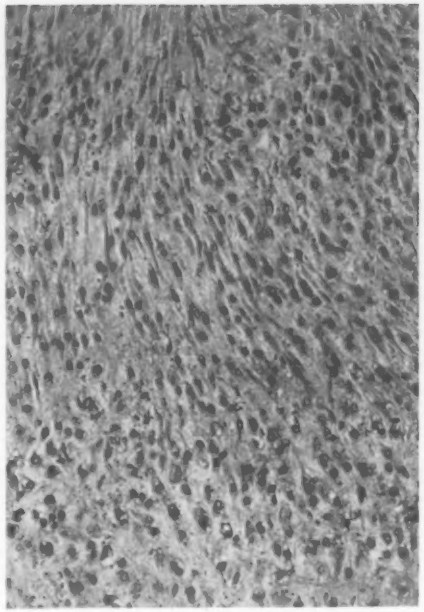

FIG. 10

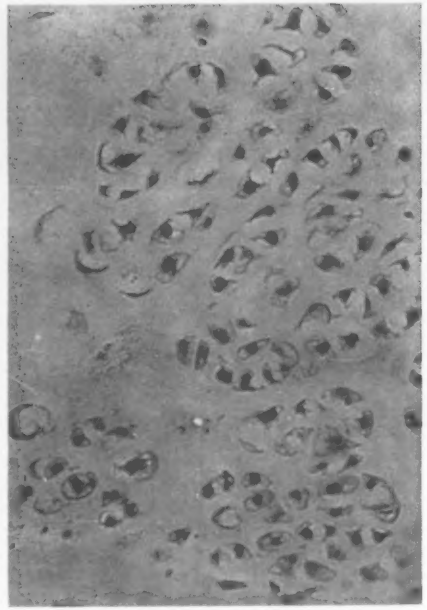

FIG. 11

FIG. 9.—(Case 7) Recurrent chondrosarcoma of ilium. Photomicrograph of last tumor excised from Case 7 eight years after original operation. Note greatly increased size of nuclei. (x 200)

FIG. 10.—(Case 8) Chondrosarcoma of sacrum. Note absence of lacunar cells and myxomatous appearance. Case 8. (x 200)

FIG. 11.—(Case 9) Chondrosarcoma of ilium. Little is seen to suggest a malignant neoplasm yet local recurrence and pulmonary lesions appeared no more anaplastic. Photomicrograph Case 9. (x 200)

remained elevated, the blood pressure fell off gradually. Examination showed spasticity of the extremities and bilateral positive Babinski reflexes. She did not rally and expired on July 2, 1941.

Pathologic Examination.—The specimen consisted of numerous irregular pieces of friable, pink-gray cartilaginous tissue having a combined weight of 955 Gm. Some of the larger masses contained crateriform spaces with ragged walls.

Histologic examination revealed moderately atypical cellular hyalin cartilage with abundant basophilic matrix. Lobulations were distinct. Stellate and fusiform cells with small compact nuclei predominated at lobular peripheries but ovoid lacunar cells were found in the more central portions. The ovoid cells had vacuolated cytoplasm. Some of

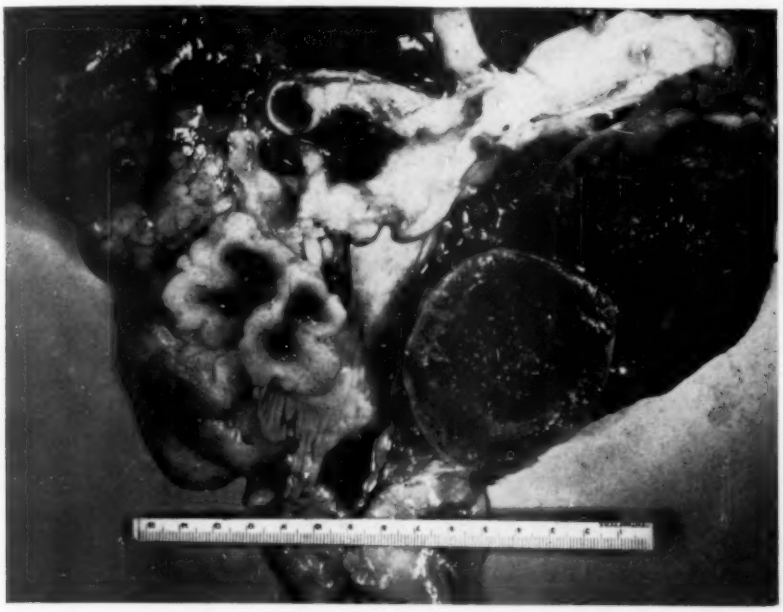

FIG. 12.—(Case 9) Lung containing old chondroid lesion of lower lobe known to have been present at least 4 years. The smaller irregular masses probably represent metastases from a chondrosarcoma of the ilium. (Case 9)

them approached "signet ring" types with a large central vacuole surrounded by a thin rim of cytoplasm containing a flattened nucleus. The other ovoid cells had small round or ovoid granular nuclei with one to three distinct nucleoli. Only a few relatively large nuclei could be found and there were no binucleate cells, tumor giant cells or mitotic figures. Some of the pieces appeared to be definitely encapsulated by moderately vascular connective tissue which contained a few tiny well formed spicules of bone (Fig. 11).

At postmortem examination a large mass of soft, friable cartilaginous tissue replaced much of the posterior portion of the right iliac bone. The mass contained cysts with ragged walls from which yellow, serous fluid escaped. An encapsulated red-brown, fluctuant mass 6 cm. in diameter lay near the medial aspect of the base of the right lower pulmonary lobe. Clear amber syrupy fluid escaped when the mass was cut leaving a firm ragged dark red wall 4 mm. thick in which focal areas of gristle could be seen. A second circumscribed mass 4 cm. in diameter lay in the posterior portion of the middle lobe of the right lung. It was firm and its cut surfaces were pearly white with a central area of green-red necrotic material. Two other pulmonary masses of similar character, each 2 cm.

in diameter, were found nearby. No connection with bronchi could be demonstrated in any of the pulmonary lesions (Fig. 12).

The pelvic mass was distinctly more cellular than formerly and the matrix, while essentially hyalin, appeared stringy and foamy. Lacunae were well formed. Most of the cells were ovoid with small dark nuclei but a few stellate and spindle-shaped cells were found in lobular peripheries.

Tissue from all of the pulmonary masses appeared similar histologically. They were completely encapsulated masses of atypical adult type hyalin cartilage. The cells varied in size but all were ovoid with small dark nuclei and lay in lacunae. The matrix was well formed. The largest mass was partly calcified.

Another pertinent finding at necropsy was bilateral massive adrenal hemorrhage.

Case 10.—No. 248107, W. S., widower, age 46, was admitted to the Rochester Municipal Hospital, May 17, 1946. He was in good health till seven weeks ago. At that time he had a sharp pain in his right lower thigh. The pain lasted for a short time and recurred about two weeks later. He found a mass the size of his fist on the iliac bone. One week ago he had a pulling sensation in his right testicle and a dull aching pain in his right thigh. He consulted his doctor who took x-rays and referred him to this hospital. He had lost eight pounds in a year but did not know when.

In his past history he had been healthy. He had had no disease of any sort. His family history had no bearing on the present illness.

Examination revealed a well developed and well nourished man. He was in need of some dental care for cavities. He had a blood pressure of 180 systolic/100 diastolic. There was a bony hard mass in the right lower quadrant fixed to the crest of the right ilium. It measured 15 cms. in diameter and was smooth, rounded and slightly tender. The external border of the ilium was thickened but the major part of the tumor extended medially and posteriorly toward the sacro-iliac joint.

Laboratory studies showed red blood cells 5,210,000, white blood cells 7,000, hemoglobin 16 Gm. The platelets and the differential count were normal. The Wassermann reaction was negative. His blood contained calcium 10.2 mgs. per cent; phosphorus 4.0 mgs. per cent, acid phosphatase 2.1 and alkaline phosphatase 5.9 King-Armstrong units. Roentgenograms of the chest were negative for metastases. The right ilium in its posterior portion contained a tumor mass which measured 9.0 x 10.0 cms. This consisted of clear zones surrounded by patchy dense calcified areas, irregular in outline and ragged in appearance. It was a typical chondrosarcoma. The lesion extended almost to the transverse process of the 5th lumbar vertebra.

On May 22, 1946, a wedge of ilium was taken out giving a good margin to the tumor all around it. It was necessary to remove the transverse process of the fifth lumbar vertebra in order to get access to the tumor. A bridge of bone was preserved from the sacro-sciatic notch to the sacrum. The peritoneum was not entered but pushed aside to expose the growth. The tumor had extended posteriorly under the gluteus muscle. The muscle bundles were divided down to the bone which was exposed all the way to the sciatic notch. Closure was made in layers with silk. The operation took three hours. Ether anesthesia was used. Transfusion of 1,500 cc. of blood and 700 cc. of normal saline was employed throughout the operation. There was no shock. He had retention of urine postoperatively. It was necessary to put him on constant drainage. Sulfadiazine was given. He developed a wound infection and an abscess in the dead space. This was drained. *B. subtilis* was cultured from the pus. His wound was treated by hot compresses and he was given penicillin. The wound granulated and slowly healed. He was discharged on July 15, 1946, to get about on crutches. On Aug. 5, 1946, he was in excellent shape. He had an aching sensation on sitting but no pain elsewhere. He had not borne weight but roentgenograms taken as check films postoperatively showed a surprisingly good bridge of bone which appeared to be substantial enough to stand stress.

FIG. 13.—(Case 10) Chondrosarcoma of ilium, posterior view. Case 10

He was readmitted on Nov. 6, 1946. He had gained 30 pounds since his previous admission. There had been pain in the course of his sciatic for about one month. A mass, which felt hot, was noted near the anterior superior spine about one week previously. It was excised with a wide margin and a portion of the ilium taken with it on Nov. 11, 1946. Following this operation he suffered with sciatic pain and numbness and tingling over the plantar surface of the foot. A myelogram showed a space displacing mass at the 5th lumbar disc space. This area was explored on Dec. 23, 1946, and a metastatic nodule was found. Bilateral chordotomy was done under local anesthesia at the level of 3–4 and 5th thoracic vertebrae on Jan. 8, 1947. This gave him freedom from pain. He had incontinence of bowels and bladder for some weeks after operation. The bowels gradually improved but it was necessary to do a suprapubic cystostomy on Feb. 27, 1947. Paraplegia developed gradually and a mass appeared in the right lower quadrant of the abdomen. Exitus occurred June 12, 1947.

Pathologic Examination.—The original specimen consisted of the posterior two-thirds of the right ilium including the sacro-iliac joint and a strip of sacrum 1.5 cm. wide. Globular firm masses protruded from the medial and lateral surface of the ilium. On frontal section the central third of the bone was replaced by a firm, gray mass which spread beyond the bone conforming to the outline noted on external examination. The entire tumor measured 15 x 10 x 8 cm. It was circumscribed but not encapsulated. The superior and inferior thirds of the mass were gray, translucent, lobulated and firm, obviously cartilaginous. A cystic space 3 cm. in diameter filled with partly clotted blood was seen at the superior pole and the tissue about this area was yellow-gray and soft. The middle third of the neoplasm was less cartilaginous containing irregular areas of opaque, yellow-gray gritty material. The ilium adjacent to the lesion was eburnated (Fig. 13).

On histologic examination the major part of the tumor was composed of atypical adult type hyalin cartilage with well defined lacunae and basophilic homogeneous matrix. The cells were generally small but varied widely in shape. Nuclei were small and compact. No tumor giant cells or mitotic figures were found. Binucleate cells were seen rarely. Areas of necrosis and calcification were found in many sections. Myxomatous foci were encountered infrequently (Fig. 14).

An entirely different picture was seen in sections taken from the periphery of the middle third of the neoplasm where numerous spindle-shaped cells of variable size formed a network about endothelial-lined blood spaces. This tissue invaded bone and adjacent soft parts. Several small foci of similar appearance were found in sections taken from widely scattered areas leading one to believe that this type of reaction may have been multicentric in origin.

A third type of tissue, more anaplastic than the others, was found about the blood-filled cyst where closely packed spindle-shaped cells formed a poorly fasciculated mass. There was marked variation in nuclear size and shape. Hyperchromatism was pronounced. Mitotic figures and tumor giant cells were seen. Collagen was present in small quantities. The edges of this tissue lay next to atypical hyalin cartilage but there was no evidence of a transitional pattern between the two (Fig. 15).

The soft parts about the tumor were generally atrophic and infiltrated with lymphocytes. No real capsule could be found. Skeletal muscle was infiltrated by typical tumor-cartilage in some regions.

The first recurrence excised from this patient was received in the laboratory as a piece of the right ilium measuring 4 x 4 cm. to which were attached skin and subcutaneous tissue. A hard spherical mass 4 cm. in diameter lay next to the lateral aspect of the bone. The cut surface of the tumor was gray marked with areas of hemorrhage and cyst formation. A circumscribed stony hard nodule 1 cm. in diameter lay in the subcutaneous tissue about 1 cm. from the larger mass. This had a red-gray cut surface.

Tissue from the larger mass contained interlacing bundles of spindle-shaped cells which varied markedly in size. Collagen was plentiful. The smaller mass contained only

poorly outlined ovoid cells with homogeneous or finely vacuolated ambophilic cytoplasm and large vesicular nuclei. There was no intercellular material. Areas of hemorrhage and necrosis were seen. Tumor giant cells and bizarre mitotic figures were found in both of the tumors which infiltrated soft tissue. The bone contained no neoplastic cells (Fig. 16).

The second recurrence was macroscopically nondescript. The histological characteristics were similar to the highly vascular multicentric part of the parent lesion. Spindle shaped and polyglonal cells formed a network about endothelial lined spaces. Variation in cell size and shape, hyperchromatism and mitotic figures were conspicuous (Fig. 17).

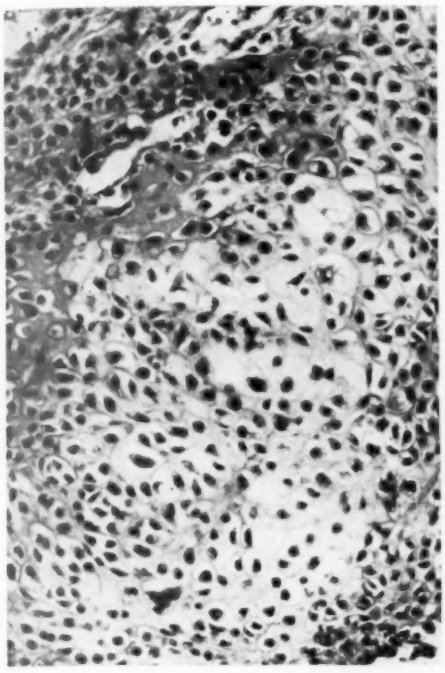

FIG. 14

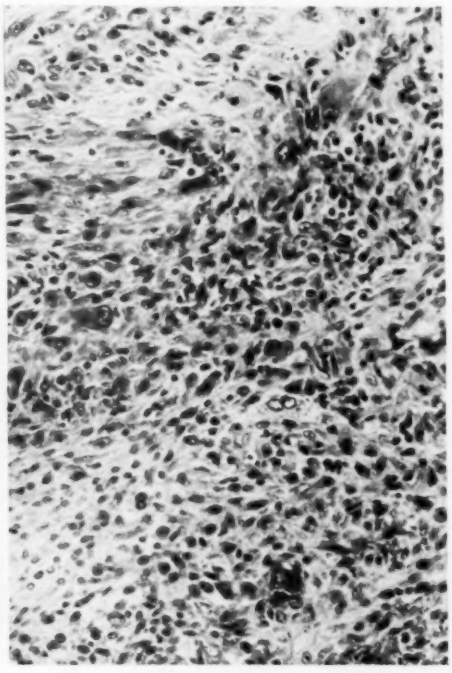

FIG. 15

FIG. 14. (Case 10) Representative area of cartilaginous component of chondrosarcoma of ilium. (x 200)

FIG. 15.—(Case 10) Area of anaplastic sarcoma from chondrosarcoma of ilium. (x 200)

A gray resilient extraperitoneal mass weighing approximately 2 kg. filled the surgically created defect in the ilium at postmortem examination. The tumor extended from the ilio-lumbar ligament to the conjoint tendon encroaching on the pelvis. Neoplastic tissue invaded the last two lumbar vertebrae and the upper portion of the sacrum. Tumor thrombi were found in the iliac arteries and veins which were distorted by the mass. A solitary metastasis 3 cm. in diameter was seen in the liver and smaller nodules of tumor were found in the lungs and the right kidney.

All of the structural patterns observed in the surgical specimens of the neoplasm were found on histologic examination of the autopsy material. Only a few of the lung metastases were frankly chondroid. All of the other lesions resembled poorly differentiated fibrosarcoma.

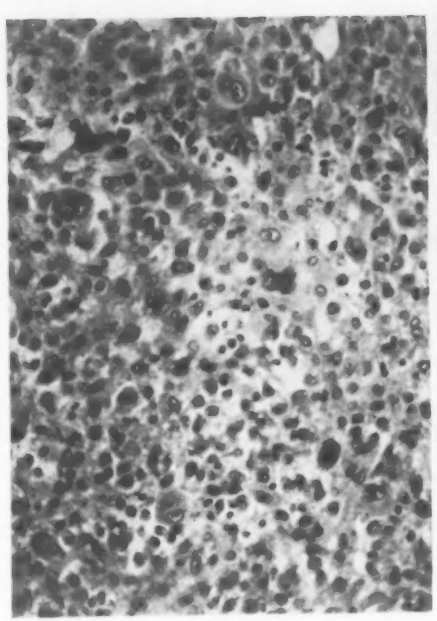

FIG. 16

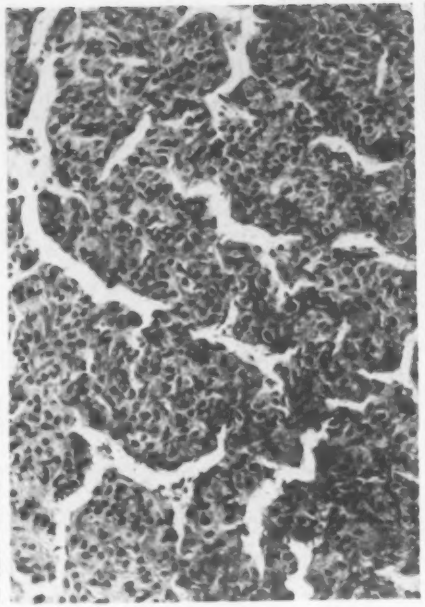

FIG. 17

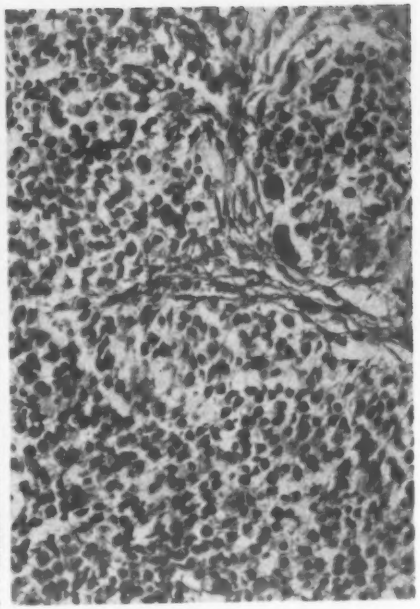

FIG. 18

FIG. 16.—(Case 10) First metastasis from chondrosarcoma of ilium. (x 200)
FIG. 17.—(Case 10) Intraspinal metastasis from chondrosarcoma of ilium. (x 200)
FIG. 18.—(Case 11) Pulmonary metastasis from chondrosarcoma of pubis. (x 200)

Case 11.—No. 43193, I. D., female, age 51, was admitted to Strong Memorial Hospital Nov. 2, 1939, because of increasingly severe pain in her right hip and knee for two years. Masses were palpable in the right lower abdominal quadrant and between the right iliac crest and greater trochanter. Motion of the right hip joint was restricted. The right lower limb was atrophic. An extensive destructive lesion about the acetabulum was demonstrated on roentgen examination. A course of roentgen therapy to the hip did not influence the size of the tumor.

Right interinnomino-abdominal amputation was performed in January, 1940. Convalescence was complicated by wound infection but the patient was in good general condition when she left the hospital two months after operation. In January, 1941, roentgenograms of the chest revealed extensive metastases and death ensued one month later.

Pathologic Examination.—The surgical specimen consisted of the right lower extremity and the right innominate bone. An ovoid, coarsely nodular, elastic mass 18 x 12 x 10 cm. arose from the upper ramous of the pubis above the obturator foramen extending medially and laterally. On cut section the upper part of the pubic ramus was a poorly defined mixture of chalky bone and cartilage. The neoplasm extending from the bone was translucent, gray and rather soft. Some areas were gelatinous. The acetabulum was replaced by tumor and gelatinous material was found in the hip joint. The external aspects of the tumor were covered by tough fibrous tissue continuous with the periosteum but the lesion was not truly encapsulated.

Cellular pleomorphism and poorly formed matrix characterized this neoplasm. Large round or oval cells and smaller fusiform or stellate cells were mixed together. The nuclei were relatively large. Cytoplasm was acidophilic, homogeneous in the smaller cells, vacuolated in the larger ones. Many cells contained two or three nuclei and true tumor giant cells were found. Mitotic figures were encountered infrequently. The watery-appearing matrix contained fine acidophilic fibrils. Occasionally one found small islands of basophilic hyaline ground substance. Lacunae were absent. The tumor was enclosed in a moderately vascular capsule from which septa ran a short distance into the neoplasm but lobulation was not a conspicuous feature in this lesion.

At postmortem examination a large tumor mass weighing approximately 4,000 Gm. filled the right lower quadrant of the abdomen. It measured 22 x 20 x 18 cm. after a large amount of thick, brown glutinous fluid had escaped from its central cystic portion. The cut surfaces of the mass were firm gray and glistening except for the cystic areas. The mass was firmly adherent to the surrounding structures, infiltrated the gluteal muscles, and surrounded and invaded the resected portion of the sacrum.

The right iliac vein was occluded by tumor thrombus which extended to the lower end of the inferior vena cava. Similar thrombi occluded the larger pulmonary arteries. Grossly visible metastases were seen in the lungs, bronchial lymph nodes, kidneys and spleen.

On microscopic examination the neoplasm found at autopsy was extremely cellular and almost devoid of matrix. The cells were round with large granular nuclei, inconspicuous nucleoli and either finely granular or vacuolated cytoplasm. Hyperchromatism was moderate. Mitotic figures and tumor giant cells were conspicuous. The tumor infiltrated muscle and adipose tissue. The metastases were usually circumscribed but some infiltrated adjacent structures. All of them had the same cytologic characteristics as the pelvic mass (Fig. 18).

Case 12.—No. 161737, M. M., white, male, age 54, was admitted to the Strong Memorial Hospital, Feb. 1, 1940, complaining of pain in the right hip for the past eight years. A tumor had been curetted away from the region of the greater trochanter in 1936 at another hospital. This was followed by roentgen therapy. The lesion recurred slowly, pain became increasingly severe and the hip joint stiff. A huge mass involving the upper left thigh and pelvis was palpable. The left hip was held in 45° fixed flexion and the lower limb was atrophic. There was a draining sinus in the old operative scar. Roent-

genograms revealed a mass surrounding the femur in the trochanteric region with partial destruction of the femur, pubis and ischium.

Modified interinnomino-abdominal amputation was performed Feb. 7, 1940, from which the patient made a splendid recovery being discharged from the hospital 60 days after entry. Recurrent tumors were excised from the operative site in August and October, 1940. In December he returned to the hospital because of a lump in the left tenth rib which was excised *en bloc*. Widespread metastases eventually appeared and the patient died Oct. 3, 1941. Permission for postmortem examination could not be obtained.

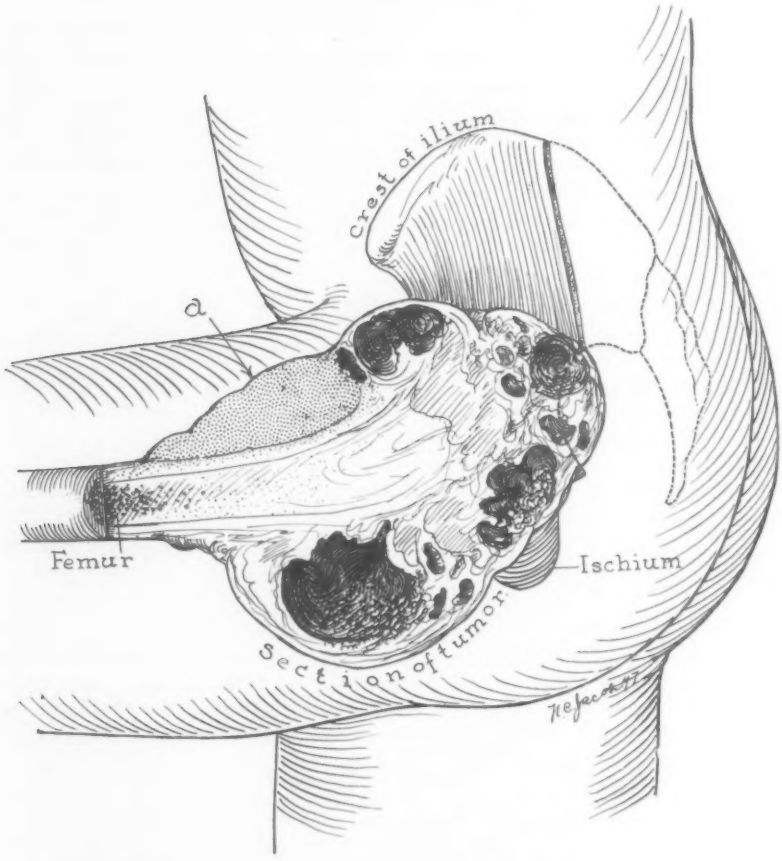

FIG. 19.—(Case 12) Chondrosarcoma of hip Case 12. The stippled area *a* contained histologically typical osteogenic sarcoma. The rest of the mass was frankly chondroid including the intramedullary extension in the femur.

Pathologic Examination.—Tissue removed at operation in 1936 contained fragments of atypical hyalin cartilage. Cells were generally ovoid or spindle shaped and the matrix was poorly formed. The nuclei were small and compact. Binucleate forms were seen rarely.

The specimen received after interinnomino-abdominal amputation consisted of the left half of the pelvis and attached lower extremity. The medial half of the pelvis was covered by a gray bosselated tumor mass 20 cm. in diameter which extended over the hip joint to the junction of the upper and middle thirds of the femur. The middle third of the femoral shaft was almost twice the diameter of the lower third. The consistency varied.

It was generally firm and elastic but the posterior inferior portion was boggy and that part overlying the ventral surface of the femur in the region of the greater trochanter was stony hard. On section through the pelvis and femur the bulk of the mass was gray, translucent and glistening, obviously cartilaginous. There was a blood-filled excavation 6 cm. in diameter in the posterior inferior aspect of the tumor, and the hard area noted above appeared white and fibrous. Part of the ischium and pubis was destroyed and replaced by a mixture of calcareous material and chondroid tissue. Cortical bone in the upper third of the femur was 1 cm. thick. The medullary cavity was filled with cartilage. The relationships of the various parts of the lesion are shown in Figure 19.

The great bulk of this tumor was composed of atypical cellular hyalin cartilage in which cellular pleomorphism was conspicuous. Relatively large vesicular nuclei were the rule. Many binucleate forms were present but neither tumor giant cells nor mitotic figures were found. There were large areas of necrosis and irregular deposits of amorphous calcific material. Some nodules were made up of typical myxomatous tissue in which the cells had small round nuclei. The mass was partly surrounded by dense, avascular collagenous tissue from which short septa extended into the tumor, but, in general, lobulation was poorly defined.

Sections taken from the hard white area near the greater trochanter of the femur appeared entirely different. The cells were generally spindle-shaped with hyperchromatic nuclei. Mitotic figures were readily found. Little collagen was seen but many spicules of poorly formed bone were imbedded in the sarcomatous matrix. Much of the tissue was necrotic. Frankly cartilaginous tissue lay next to areas of typical osteogenic sarcoma. Soft tissues about the lesion were compressed but not invaded by tumor.

Local Recurrence.—This resembled the more cellular areas of cartilage seen in the parent tumor. Matrix was scanty; cells, pleomorphic; and nuclei large, though few mitotic figures and no tumor giant cells were seen.

Lesion from Rib.—This appeared almost identical with the sections taken from the trochanteric region—frank osteogenic sarcoma.

Case 13.—H. F., No. 224081, a 33-year-old married woman, was admitted to the Strong Memorial Hospital on October 2, 1944. She had been a hospital patient in another city since February 3, 1944. Her trouble began six years previously, following the birth of a son. At that time a mass was noted in her pelvis causing her to limp on the left leg. It was decided to try radiation treatment and two courses of deep therapy were given without benefit. She began to get flexion and stiffness of the left hip. In the spring of 1941 she developed malaise, severe nausea, vomiting, and constipation. A colostomy was performed in June of 1941. She was in the hospital for two months. At home she remained in bed another two months and then got about on crutches to a slight extent. After this, she was confined for a period of six months to a sanitarium for general care. She was returned to the general hospital because of urinary retention in February, 1944. A biopsy of the tumor was taken and a diagnosis of chondrosarcoma was made. A second course of radiotherapy was given without noticeable result. She remained on catheter drainage. In April, 1944, an 8-inch incision was made in the left inguinal region and a part of the cartilaginous growth was removed. The surgeon decided that the tumor could not be removed and further attempt was given up. The wound became infected and was left open for drainage. From the time of onset in 1939 there had been progressive loss of sensation and motor control in the left lower limb until she had complete paralysis and sensory loss below the hip joint level.

In her past history there had been little of significance until her present illness. Since 1941 she had had a colostomy which was well regulated until June, 1944. Since that time she had had poor control with large normal-appearing stools per rectum at times. She had had urinary frequency, dysuria, and passage of rather thick purulent material. Her menses had stopped following the x-ray treatments. She had had occasional sharp shooting pains into the left leg.

Her family history was important in that her mother had died of cancer of the breast with metastases in 1937. Her father died in 1916 of a bone disease of the spine, possibly tuberculosis. There was a history of cancer in an aunt and an uncle, the aunt being her mother's sister who died in 1937. The uncle married into the family.

She had the appearance of a chronically ill patient, poorly developed, emaciated, incapacitated. She was cooperative and intelligent. She had pallor of the skin, clubbing of the fingers and toes. The left hip was held in an acutely flexed position at a 45° angle. It was not possible to extend the thigh, but a slight amount of rotation was obtained. The lower leg was flexed and rotated outward. There was loss of muscle power, atrophy, and loss of superficial pain and touch in this limb though deep pressure and vibratory sense were retained. Hip flexion and knee flexion contractures were of considerable extent. There were ulcerations on the left heel. The deep reflexes were not obtainable. A bony hard tumor mass was palpable, extending from the symphysis across the whole left abdomen above the left ilium and around to the sacrum in back. It invaded the gluteal muscles extensively. The abdomen was asymmetrical as the whole left lower portion bulged with a prominent tumor. There was a colostomy opening at about the level of the umbilicus on the right. In the left groin there was a 6-inch (15 cm.) gaping wound which was discharging purulent material. Pelvic examination indicated that the rectum and vagina was pushed to the right side of the pelvis. Her temperature was 97.7°F (36.5°C), pulse 98; blood pressure 88 systolic, 48 diastolic. She weighed 88 lbs. (40 kilos.). The white blood count was 6,100 and the hemoglobin was 10.6 Gm. Her total proteins were 5.44 per cent with 3.56 per cent serum albumin and 1.88 per cent serum globulin. Blood chlorides were 562 mgs. per cent; nonprotein nitrogen 27 mgs. per cent. The urine contained large numbers of pus cells and grew *Staphylococcus aureus hemolyticus* on culture.

The x-ray appearance was typical of chondrosarcoma (Fig. 20).

She was placed on mandelamine in an attempt to clear the urinary infection. She could not take the sulfa drugs as she had a susceptibility which had been determined on her other hospitalizations. She was given a high caloric diet and the infected wound was compressed. Her colostomy was not functioning well and had to be regulated. This therapy took about three weeks, after which it was decided to attempt operation.

An incision was made just to the left of the mid-line from the symphysis to beyond the umbilicus. Many adhesions were freed. The tumor extended across the pelvis into the right iliac fossa. It ran close to the base of the bladder. The uterus was pushed over to the right, the left round ligament being greatly stretched. This was divided. The left tube and ovary were normal, the right ovary was not present. The right ureter was normal. The left ureter ran into the tumor mass and could not be traced. The rectum was full of very hard fecal material, the colostomy being apparently an opening into the side of the transverse colon and not an obstructive type. On the medial side of the rectum there was a mass of gelatinous-like tissue resembling colloid. There was no induration of any sort, but it was decided to take a biopsy in order to rule out colloid carcinoma. The left common iliac artery was exposed and doubly ligated with cotton. This artery was much smaller than the corresponding iliac artery on the right. Closure was made in layers with cotton. The operation was well tolerated. It seemed that a resection might be possible although it was debatable. Many of the staff were positive that the condition was inoperable, a view with which I was in complete accord. The patient and her husband, however, wanted to take any risk as they had nothing more to look forward to. Accordingly on November 1, 1944, eight days later, an inter-innomino-abdominal amputation was carried out. It was necessary to modify the usual operation in several particulars. First, an incision was made in the left groin parallel and medial to the infected incision left by the operation of April, 1944. A flap of skin and subcutaneous tissue was turned over and sutured to the iliac crest completely covering the infected area. A new aseptic procedure was then instituted. A second incision was made through the abdominal wall between the mid-line and the previous inguinal incision. Thin adhesions were separated easily. The symphysis was divided. The tumor extended directly under the urethra from which it was

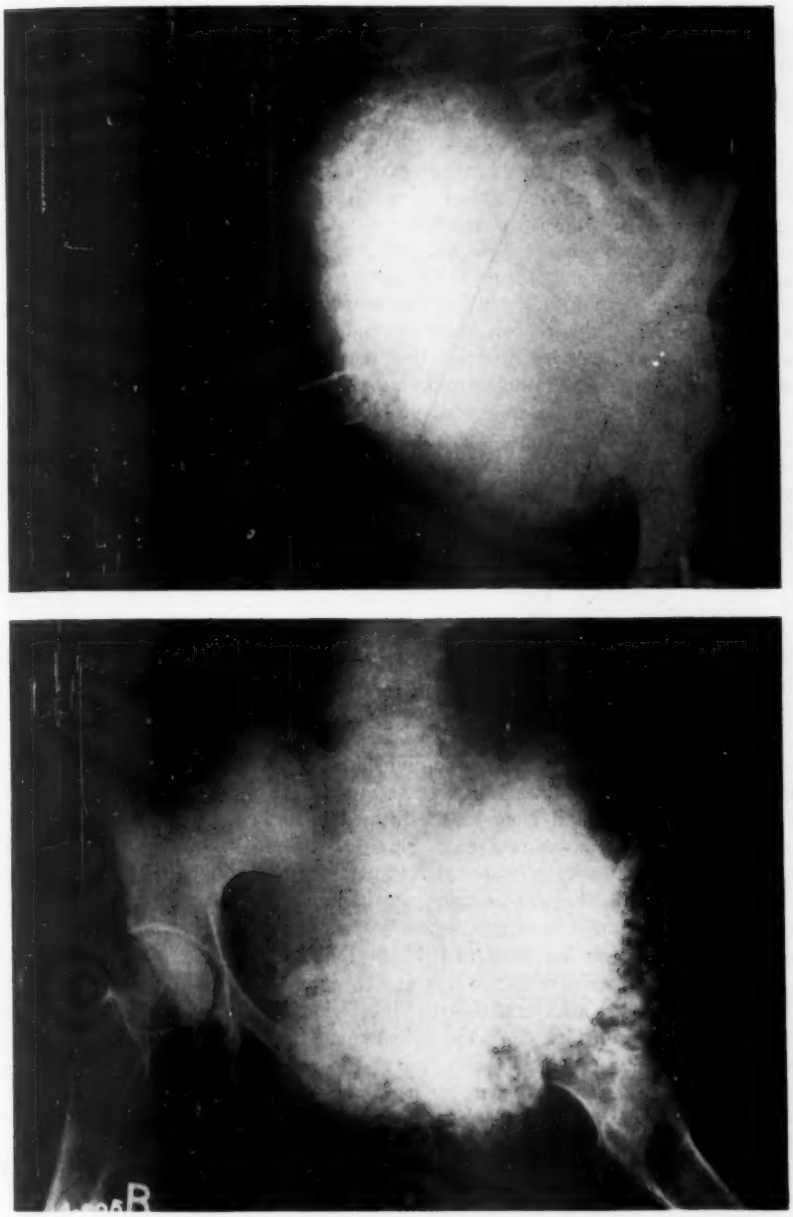

FIG. 20.—(Case 13) Roentgenographic appearance of huge chondrosarcoma of ilium. (Case 13)

dissected free. A pin-point opening was made into the urethra in spite of every precaution. It was repaired at once. The vagina had been pushed over to the right by the tumor. It was entered at one point, but no attempt was made to close it. The left ureter was clamped and divided below the tumor where it entered the bladder. It was identified above the tumor, divided and tied. It contained some whitish cloudy fluid. (Intravenous pyelogram before operation showed no filling of the left kidney pelvis). Then, the patient was turned over on her abdomen, the orthopedic trough making this easily accomplished. It was apparent that the tumor had invaded the gluteal muscles almost everywhere and that these structures could not be used for closure. A flap of skin and subcutaneous tissues was developed from the antero-lateral side of the left thigh and from behind the iliac crest to the mid-line spines posteriorly. This flap was turned over toward the right side. The femoral nerve and the ilio-psoas and levator muscles were divided. The rectum was dissected free from the tumor and pushed to the right side of the pelvis. The sciatic nerve and all the other structures holding the limb were cut across, the incision passing through the left sacro-iliac joint into the great sacro-sciatic notch and across the lower sacral segments. A portion of the left lower sacrum and the coccyx had to be sacrificed with the sacrum. Closure was made by swinging the posterior flap to the incision on the anterior abdomen. The rectum was sutured back into its normal relations. The operation was deliberately performed with a minimum of blood loss under nitrous oxide—ether anesthesia. It took 4½ hours. There was mild shock after the second hour but with saline and blood intravenously the pressure was on the rise before the operation was completed.

The postoperative course was complicated. She had purulent drainage from the vagina immediately postoperatively. On the 5th postoperative day several firm fecal masses were removed from the rectum, the patient having desire to defecate but not being successful. She had been placed on constant bladder drainage. On the 6th postoperative day she complained of pain similar to that in the left leg before operation. She thought the limb was undergoing twitchings or gentle flexion and extension of the thigh. These sensations were not very troublesome usually. However, upon some manipulation such as a dressing or an enema the phantom limb sensations became especially vivid and distressing. She might have a shooting pain to her leg and foot on these occasions. All sutures were removed on the 12th postoperative day. The wound was well healed without infection. There was a slight reddening of the skin flap over the divided edge of the sacrum. She was kept comfortable on codeine and bromides. An abscess formed in the posterior part of the incision and *B. proteus* was cultured from it. It drained profusely. Another pocket was found over the sacrum. These abscesses healed slowly but were healed by the 6th week after operation. She had difficulty with her urinary tract and vaginal infections for about the same length of time. She began to get up on crutches in the 5th postoperative week. This caused her to feel her amputated limb again, in a flexed position as previous to operation. She said that it made her feel tired to hold the limb in this position. She began to gain weight and strength. Her appearance was greatly improved. The colostomy opening continued to annoy her. So after studying the bowel by barium through the colostomy and by rectum, it was decided to close the colostomy. The colostomy was excised and an end-to-end anastomosis made on January 18, 1945. Spinal anesthesia was used. The phantom limb had not been prominent for a couple of weeks. But when she was brought into the operating room after the spinal anesthesia had been given she complained of tingling, "pins and needles" sensations in the limb. She said that it was straight out,—full length. She cried out with sharp pain in the knee joint of this limb. She apologized and said: "It is foolish. I know there is no limb there." This sensation lasted about 10 minutes while she had anesthesia to well above the costal margin at the time. She passed gas by rectum on the 4th postoperative day. The bowel functioned normally after this. Convalescence was uneventful. She got about the ward on crutches which she managed nicely. She was discharged on February 2, 1945, much improved with well healed incisions. She had gained 25 pounds since operation.

Postoperative x-rays showed absence of the left pelvis but nothing else of note.

She was readmitted in March, 1946, for local recurrence of the lesion. It was excised and she was discharged in good condition. The tumor was .he size of a lime near the coccygeal region.

In August, 1946, she returned with small bowel obstruction. It was released. Another nodule was present back of the rectum. It was friable and broke on attempting to remove it. The area was carbolized.

The small bowel attached itself to the carbolized area and obstructed again. An enteroenterostomy between the dilated and collapsed loops of terminal ileum gave relief to her obstruction. She was discharged in good condition.

She was admitted to the hospital for the 4th time on Jan. 7, 1947. A recurrence had been noted on examination. She had had some distention with pain, referred to her phantom limb and shooting pains in the stump. Recurrent nodules were removed from the omentum, vagina, wall of the rectum and perineum. One of the recurrent nodules broke on attempting to free it. Following operation she had an infection which gradually collected as a large abscess. It caused severe shooting pain into the phantom limb. Drainage of the abscess was accompanied by complete relief of symptoms and the phantom limb no longer gave her trouble. There were evident recurrences or residual nodules still present but she was discharged for an interval to allow her to recover. It was thought better to defer surgery till her infection had completely burned out.

Pathologic Examination.—After the soft parts had been dissected away the tumor appeared as a gray bossellated mass of firm tissue surrounding almost all of the left innominate bone. Only 4 cm. of the pubic rami and a strip of the posterior ilium 6 cm. wide were uninvolved by the mass. The cut surfaces were gray, translucent, coarsely lobulated and marked with small areas of hemorrhage and irregular, stony-hard masses of opaque, yellow-gray, gritty material. Most of the osseous tissue within the mass was completely destroyed. The neoplasm infiltrated contiguous muscle and connective tissues. It extended into the ilio-femoral ligament but did not involve the hip joint.

The tumor was composed of adult type hyalin cartilage with well defined lacunae and hyalin matrix. It was moderately cellular. The cells were ovoid, small at the periphery but larger as one progressed centrally. The nuclei were generally small but in some areas they were relatively large and in these locations one encountered binucleate cells. Cytoplasm was acidophilic, homogeneous in the smaller cells, vacuolated in the larger ones. There were no tumor giant cells nor mitotic figures. Some areas of hemorrhage and deposits of amorphous calcific material were encountered. In some regions calcification was so pronounced that a peculiar osteoid appearance was noted. All of the cells in the heavily calcified areas were small and all of these areas lay toward the center of the lesion. The tumor infiltrated adjacent bone, replaced osseous tissue, and filled the marrow spaces. It also infiltrated soft tissues and had a well defined capsule in only a few areas.

A small subserosal nodule removed from the uterus at operation proved to be an implant of chondroid tumor cells.

The third part of the specimen removed from the wall of the rectum was a moderately cystic lymphangioma. The recurrences were globular masses of tumor cartilage varying from 4 to 7 cm. in diameter. They resembled the parent tumor in all particulars excepting that they were slightly more cellular. All of them contained extensive calcific areas and in the last recurrence there was one nodule which had a bony center in which well defined marrow spaces filled with fat could be seen.

Case 14.—F. S., No. 1993, a 55-year-old man was admitted to the Rochester General Hospital on Feb. 15, 1929.

He was bowling 15 years ago when he noticed a sharp pain in the calf of the right leg as he stepped forward. The calf was quite painful for the next two weeks but he kept at his work. There was no trouble following this till three or four years later. At that time there was a swelling in the calf. Roentgenograms were taken and a diagnosis of osteo-chondroma was made. There has never been any pain or disability. But during the

last year once in a while he had had to use a pillow under the leg or it would go to sleep. The swelling had grown rapidly in size during the last three months. Trousers made three months ago are a little tight now. He walks well but tires if he walks fast.

He was always healthy. The family and past histories were non-contributory.

He was overweight. The only important finding was a huge tumor of the right calf. It approached the size of a head, was bony hard and fixed.

Laboratory studies showed normal blood and urine. Roentgenograms revealed a tumor springing from the posterior edge of the right tibia in its upper third. The cortical bone was thickened and irregular; there were many scattered calcifications in the tumor which occupied the popliteal space and upper calf.

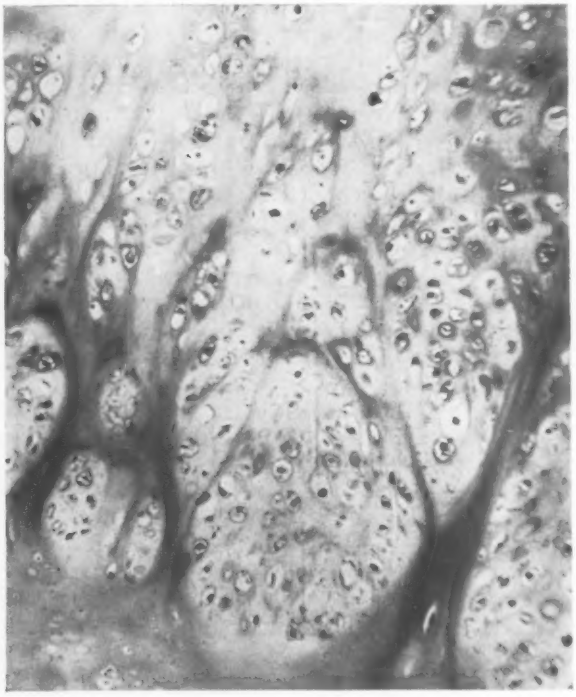

FIG. 21.—(Case 14) Chondroma of tibia. (Case 14.) (x 60)

At operation the tumor was removed locally from the tibia.

Recovery was uneventful. On Sept. 13, 1946, he had had no recurrence and was enjoying excellent health. This was over 15 years since operation.

Pathologic Examination.—The specimen was a well encapsulated, ovoid, firm, gray mass 15 cm. in diameter and 12 cm. in maximum thickness. It weighed 1,300 Gm. An irregular area of cancellous bone 7 cm. in diameter represented the base of the lesion. The greater part of the tumor's cut surfaces were made up of lobulated, gray, glistening cartilage. Many lobules had soft centers from which a viscid material could be expressed. Irregular, chalky white, gritty areas of calcification extended into the cartilage at the base of the lesion where islands of cancellous bone were also seen. The tumor was poorly delimited from the underlying bone. No capsule could be found in this region.

Histologic examination revealed characteristic adult type hyalin cartilage divided into

lobules by poorly cellular, avascular collagenous tissue radiating from the capsule. The tumor cells lay in lacunae, had acidophilic cytoplasm and small compact nuclei (Fig. 21).

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DISCUSSION.—DR. BRADLEY L. COLEY, New York: We recognize two varieties of malignant cartilage tumors which have different characteristics, such as age-incidence, growth-rate, roentgenographic findings and microscopic appearance. They also have a different prognosis and may require different treatment.

The first of these, occurring in childhood or adolescence, is a highly malignant tumor from the start and, despite amputation, a large percentage of the patients will die of metastasis to the lungs. This form resembles osteogenic sarcoma on the x-ray film and often cannot be differentiated until microscopic sections have been examined. It is termed primary chondroblastic sarcoma.

Doctor Morton's cases, however, fall into the second group which develop on a pre-existing benign cartilage tumor or chondroma, either of central or cortical origin. They are termed secondary chondromyxosarcoma, although the myxomatous element varies greatly and is probably not important.

In the second group the tumor has a more insidious onset. It may be difficult if not impossible to determine just when it ceases to be benign and becomes definitely malignant. We believe that in some instances years may lapse before this transition takes place. This tumor is radio-resistant.

It is our conviction that the presence of a benign chondroma is an indication for removal while it is still a chondroma; this may be regarded as effective cancer prevention. Conservative surgery at this early stage may be sufficient, whereas after a malignant transformation has taken place even an amputation may be ineffectual.

I shall show slides of four patients. In two the tumor was removed while it was still histologically benign chondroma; in the other two, the microscopic diagnosis was that of

chondrosarcoma. In all four cases the treatment instituted avoided amputation; in three the follow-up period exceeded nine years.

Case I. Central chondroma; appearance in 1930. Subsequently three separate attempts were made to cure by curettage but each was followed by recurrence. (2) Segmental resection of middle of humerus. (3) Appearance 18 months later. This patient has remained well for ten years.

Case II. Chondromyxosarcoma of scapula; view taken in 1935. Total scapulectomy performed 11 years ago. Patient is now well with a useful arm.

Case III. Chondrosarcoma developing in a pre-existing osteochondroma attached to the femur by a rather narrow pedicle. (2) appearance after local removal of the tumor, saucerization and chemical cauterization of the base. Patient remains well nine years later.

Case IV. Central chondroma of humerus in a 33-year-old naval officer. Appearance after five operations and immediately prior to the sixth. (2) Resected specimen 15 cm. in length. (3) Appearance nine days after a tibial transplant to replace the resected area of the humerus. This is a recent case operated upon only 16 days ago. Histologic diagnosis—benign chondroma.

We are indebted to Doctor Morton for presenting this group of cases of a type in which most of us have found in the past that the treatment rendered has been too little and too late. Later on when operations of greater magnitude have been attempted the results have been unsuccessful. Chondroma must be regarded as a disease possessing serious potentialities.

DR. KELLOGG SPEED, Chicago: My recorded experience covers ten benign chondroma, six of which were the so-called enchondroma of the bones of the hand and foot, and seven malignant chondrosarcoma, including one of the chest well previously reported before this Association. Two were of the ilium, for which I performed interilio abdominal amputation; the remainder were in the femur.

Two concise statements of Doctor Morton are noteworthy: "The microscopic anatomy of chondrosarcoma is extremely variable" and "Many sections are essential." Only by such means may the different histologic aspects, from bony tissue to soft myxomatous areas, be uncovered. Codman in 1925 referred to this distinctly in his small invaluable monograph on bone sarcoma. His opinion was that no matter what variance of tissue exists—bone, cartilage, or myxomatous, the degree of malignancy was likely to be established by the character of the undifferentiated portion of the proliferating cells, and that the gross appearance and amount of hard tissue might be misleading. This is verified by Doctor Morton's report, where metastases showed little if any chondromatous tissue.

I wish to show slides, one of a massive slow-growing chondrosarcoma of the femur, ending fatally a year after amputation of the leg; one where amputation was refused and local excision was done with no recurrence up to three years, although chondrosarcoma was diagnoses and, finally, the end result with autopsy findings 13 years later of my patient, included by Doctor Phemister in his report.

DR. DALLAS B. PHEMISTER, Chicago: Doctor Morton mentioned my previous description of chondrosarcoma of bone. In fact, the term had been in use for more than a generation, but the Committee on the Registry of Bone Sarcoma had refused to accept it. I reported a series of cases and pointed out that they could usually be diagnosed from their roentgenologic characteristics, after which chondrosarcoma was listed as an entity in the Registry.

My experience with roentgenotherapy has been somewhat different from that of Doctor Morton, in that certain cases have responded well to x-ray. A large chondrosarcoma of the ilium, confirmed by biopsy 15 years ago and treated by prolonged and extensive irradiation, has progressed only slightly during the past 13 years and as yet there

are no detectable metastases. A central chondrosarcoma of the upper end of the humerus was extensively curetted 12 years ago and then treated by x-radiation. There has since been no recurrence, an unlikely result had there been no irradiation therapy.

Because of their slow growth and tendency to late metastases, selected cases of chondrosarcoma are suitable for treatment by wide resection and bone transplantation. Several patients have been thus treated and three have remained well for six or more years. In one case, 15 cm. of the shaft of the femur was removed and replaced by two grafts taken from the tibiae seven years ago and there has been complete restoration of function. A similar result was obtained after massive excision and transplantation for a small central chondrosarcoma of the upper diaphysis of the tibia six and a quarter years ago. In the third case, the upper third of the tibia was resected eight and two-thirds years ago and the knee stiffened by bridging the defect with a graft. Resection transplantation is an operative procedure that should be more widely practiced than is the case at present.

DR. JOHN J. MORTON, Rochester, N. Y. (closing) : I wish to thank all the discussors. I agree with them that if these tumors once recur the patients are candidates for massive resection if it can be done. In the periphery, massive resection with bone graft is excellent.

With regard to x-ray therapy, it is said in the literature that they do respond to x-ray occasionally. In a report from the Mayo Clinic, Desjardine reported two cases because they did respond to x-ray. It is the exception when they do respond, rather than the rule.

EXPERIENCES WITH A BONE BANK*

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THE PURPOSE OF THIS CONTRIBUTION is to call attention to the practicality and utility of preserving human bone in a fresh state by means of refrigeration for later use in various operations upon the bones and joints. The method has been used by my colleagues and myself on the Orthopedic Service of the Hospital for Special Surgery in New York since April, 1946 and has demonstrated its value.

PAST EFFORTS AT BONE PRESERVATION

The idea of preparing and preserving bone for later surgical use is by no means new and probably can be traced back as far as the first experiments with the use of bone transplants by Ollier, who, according to Orr grafted a piece of rabbit's bone into a man in 1859. MacEwen in 1886 had the idea of obtaining bone for transplants from amputated limbs. Poncet in 1887 reported the transplantation of a phalanx from an amputated limb to an ununited fracture of the tibia. The graft healed in place although it did not cure the condition.

In a remarkably prophetic article by Carrell published in 1912 on the Preservation of Human Tissues the author reported his experiments in an attempt to find a "method by which tissues extirpated from the amputated limb of a living animal or a fresh cadaver could be stored during the period which elapses between their extirpation and their transplantation on the patient." His experiments were made with skin, cartilage, glandular tissue and bone and the tissues were preserved in cold storage immersed in Ringers solution or plasma. He concluded that the method was feasible and would prove beneficial.

Gallie in 1918 reported the results of his experiments with the use of boiled bone transplants both homologous and heterogeneous and showed that these were in time absorbed and replaced by living bone. He used them in many surgical operations including spinal fusions and thought they served practically as well as fresh autogenous bone when complete contact of the graft with bleeding bone of the host could be obtained. He prepared plates, screws and pegs from beef bone and used them for fixation in the open reduction of fractures with good results.

Lexer in 1925 reported an end result study of a series of cases in which he had transplanted whole joints and hemi joints obtained from amputated limbs and fresh cadavers. The follow-up study showed that the grafts had survived and although the joints showed remarkable degrees of degenerative changes

* Read before the American Surgical Association, March 25, 26 and 27, Hot Springs, Virginia.

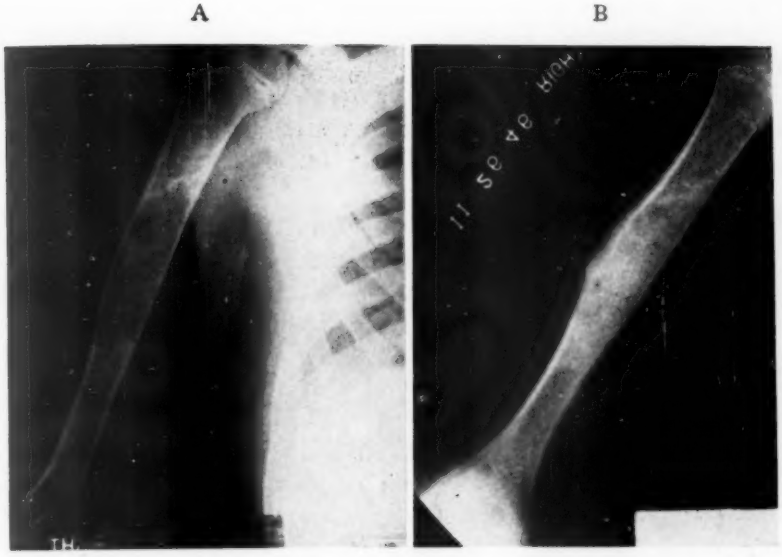

FIG. 1.—S. T. Boy, age 11 years. Recurrent Hemangioma right humerus. (A) 8–18–46 shows appearance prior to operation. Operation 9–25–46 Curettage and packing with bone chips after five days refrigeration. (B) 11–26–46—the appearance two months postoperative.

TABLE I

OPERATIONS IN WHICH REFRIGERATED BONE WAS USED

	Cases	Number of Operations
Spine fusions		
For scoliosis	7	12
For T. B. spondylitis	2	2
For congenital paraplegia	1	1
For spina bifida and spondylolisthesis	1	1
For osteochondroma of spine	1	1
For lumbo-sacral instability	1	1
Wrist fusions	2	2
Curettage and packing of bone cavities		
For osteitis fibrosa cystica		
of humerus	1	1
of femur	1	1
For fibrous dysplasia of femur	1	1
For enchondroma		
of femur	1	1
of phalanx	1	1
For hemangioma of upper ulna	1	1
Excision of osteoid osteoma of tibia and filling defect with bone chips	2	2
Débridement of chronic osteomyelitic cavities, packing with bone chips and primary closure		
of femur	1	1
of tibia	1	1
	25	30

and osteo-arthritic reaction, some of the patients had obtained excellent function.

Orrell in 1938 reported experiments with the use of chemically treated bone which he called os purum and presented cases showing the results obtained from its use for internal fixation in the fusion of joints and in osteotomies. His studies showed that boiled and dried pieces of bone were transformed more slowly into living bone than autogenous bone and sometimes were not resorbed

FIG. 2.—P. L. Man, age 32 years. Diagnosis: Old Dislocation of lunate bone. 4-3-46 Preoperative appearance. Operation 7-5-46. Excision of lunate bone and fusion of proximal carpus to radius with bone chips which had been refrigerated 15 days. 9-25-46 Results 11 weeks postoperative. Fusion is solid.

at all, probably because the coagulated and dried up connective tissue and collagen were absorbed with difficulty by the host tissues and thus prevented the revascularization of the bone. When these foreign elements were previously removed by chemical treatment the replacement was more rapid.

Inclan in 1942 reported the use of preserved bone grafts in 52 cases. Of

FIG. 3.—J. S. Boy, age 12 years. Diagnosis: Recurrent fibrous dysplasia neck of femur. (A) Operation 9–18–46 Curettage, cauterization and packing with bone chips which had been refrigerated 81 days.
(B) 11–25–46 shows preoperative appearance.
(C) 12–30–46 shows result 14 weeks postoperatively. Bone chips are healing well.

these 43 were autogenous grafts previously removed from the patient's own body with the purpose of diminishing shock and risk of infection at the time of the reconstructive surgery, eight were homologous, generally from a member of the patient's family and one was from a nine-month fetus. The bone was preserved in sterile bottles and covered with citrated blood or Ringers solution and kept at a temperature between 2 and 5 degrees centigrade. The period of preservation varied between one and 63 days. Complete success was obtained as far as the healing and physiologic action of the graft was concerned. The results were entirely comparable to those obtained from the use of fresh autogenous grafts.

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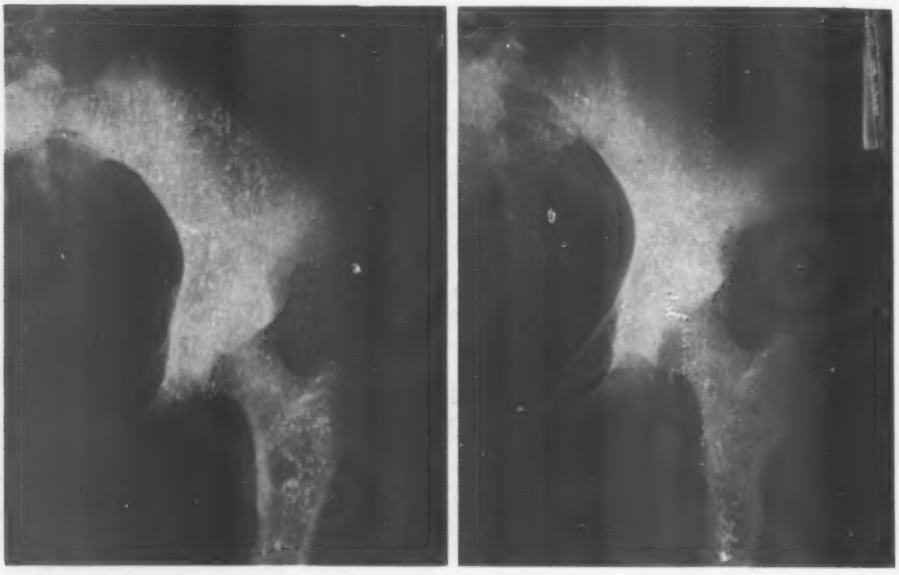

FIG. 4.—F. B. Girl, age 17 years. Diagnosis: Bone cyst of Femur. Operation 12-2-46. Curettage and cauterization of cavity, packing with bone chips which had been refrigerated 17 days.

(A) 11-14-46 Preoperative appearance.

(B) X-ray 2-14-47—Postoperative x-ray after 11 weeks. The cavity appears completely obliterated by bone.

METHOD OF BONE PRESERVATION BY REFRIGERATION

From this very brief and incomplete summary of past attempts to find substitutes for fresh autogenous grafts in surgical operations it is evident that enough success has been obtained to justify further efforts. On any active hospital orthopedic service there is constantly need of bone to be used as transplants in many different kinds of operations including arthrodesis of the various joints, surgical treatment of ununited fractures and filling of bone cavities in various types of benign bone tumors and cysts or in various conditions where excision of bone is required. Until now it has been necessary to obtain bone for such purposes by supplementary operations generally upon the

iliac crest or tibia which necessitate prolonging the time of operation, add to the operative risk and certainly increase the patient's discomfort. Not infrequently, the bone defect created by the removal of the graft often in the tibia weakens the bone to such an extent that fracture takes place at some later period.

On the other hand, many orthopedic operations such as osteotomies of the feet or of the bones of the extremities to correct deformities or certain types

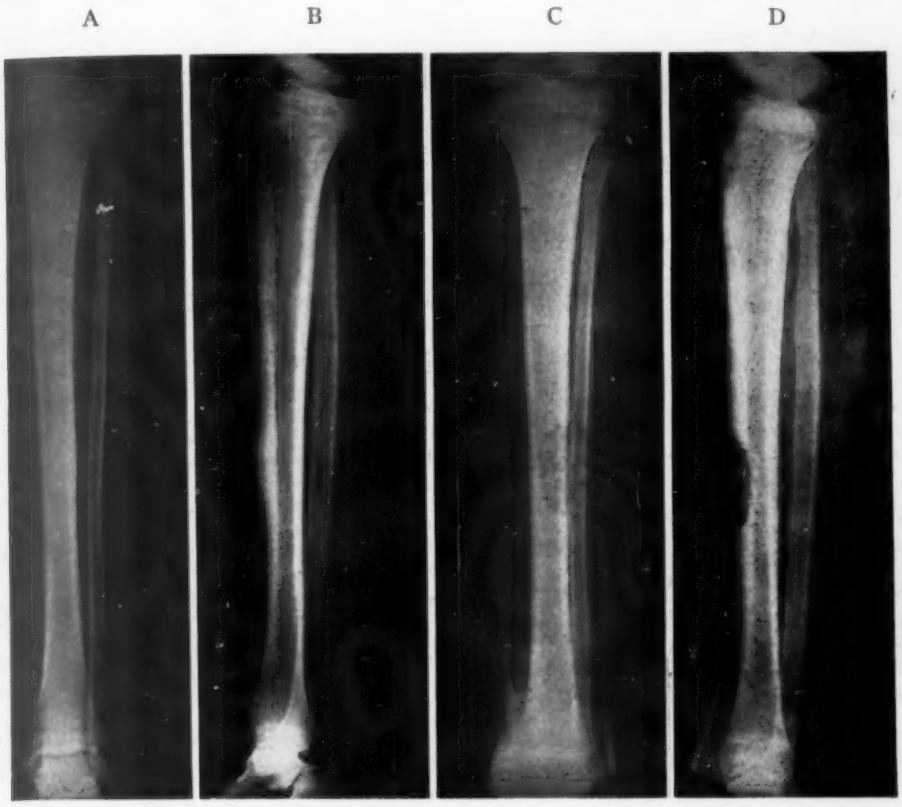

FIG. 5.—H. S. Boy, age 16½ years. (A) Diagnosis Osteoid Osteoma of tibia. Operation 12–18–46. (B) Excision of osteoid osteoma and packing of defect with bone chips which had been refrigerated 14 days. (C) 10–29–46 Preoperative x-ray. (D) 11–22–46 x-ray appearance of defect 12 weeks postoperative.

of arthroplasty necessitate the excision of considerable sections of healthy bone which until now have been discarded as of no value.

It seemed useful to attempt to preserve these fragments of bone for later use as surgical transplants and from earlier attempts and the reports of preservation of other tissues such as eyes, refrigeration seemed to offer the simplest and best method. A deep freeze unit was installed and the bone was transferred to a sterile sealed jar at the operating table and maintained at a temperature of between minus 10 degrees and 20 degrees F. No special effort was made to keep the tissue moist such as by immersing it in Ringers solution

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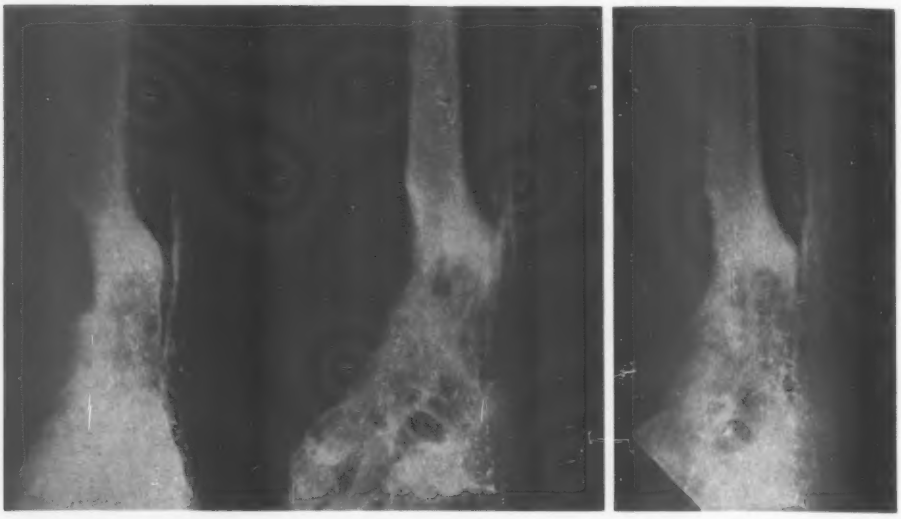

FIG. 6.—R. C. Man, age 55 years. Diagnosis: Chronic Osteomyelitis of lower tibia following compound fracture. Operation 9–9–46 Debridement of sinus and cavity, packing with bone chips that had been refrigerated 89 days. Primary closure with sliding skin flaps. (A) 9–7–46 Preoperative x-ray. (B) 11–22–46 wound healed by primary intention, the x-ray film shows the appearance 12 weeks postoperative.

A B

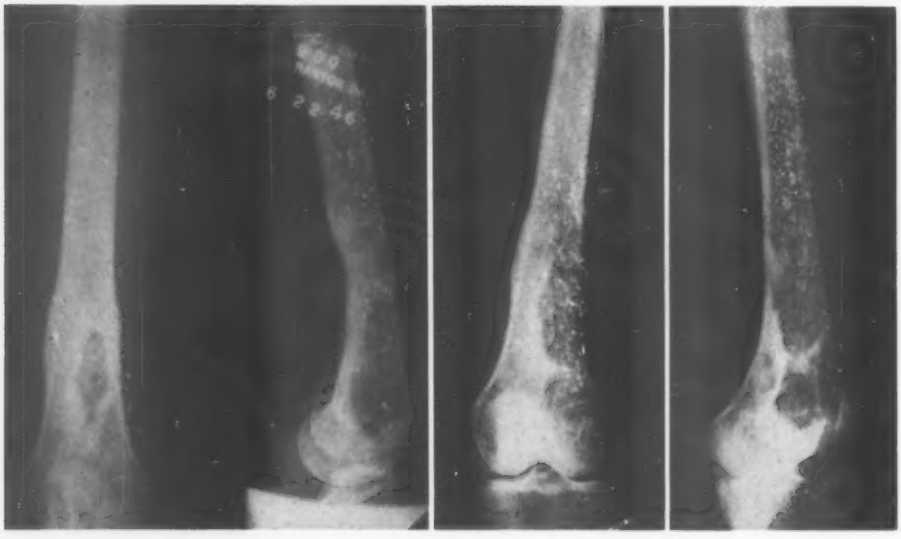

FIG. 7.—F. H. Woman, age 34. Chronic osteomyelitis lower end of femur with cavity and sinus six years duration. Operation 12–20–46. Excision of sinus, saucerization and packing of bone cavity with bone chips that had been refrigerated four days. Healing occurred by primary intention. (A) 6–22–46 Preoperative x-ray. (B) 2–8–47 x-ray appearance seven weeks postoperative. Patient has remained entirely well.

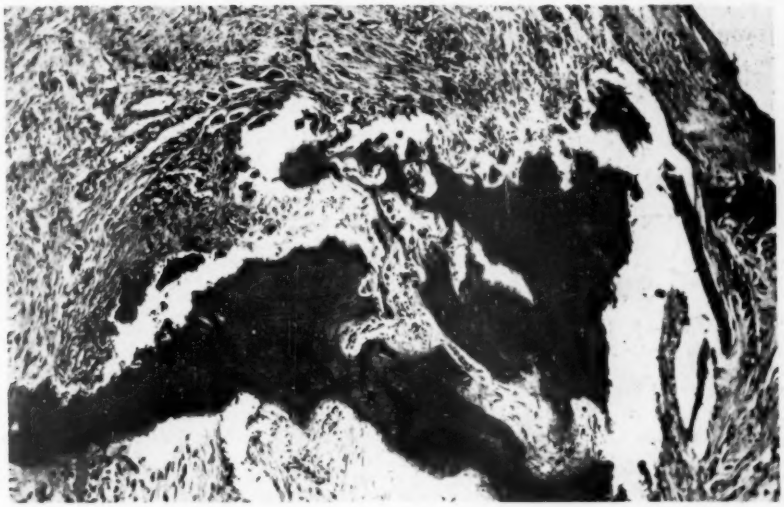

FIG. 8.—J. M. Man, age 51 years. Diagnosis: Low Back pain, lumbosacral instability. Operation 2–17–42. Spinal fusion with autogenous bone chips. Died of coronary thrombosis 3–12–42 (23 days). A section of the healing autogenous graft is shown and the appearance is that of resorbing dead bone and replacement by living bone from the host.

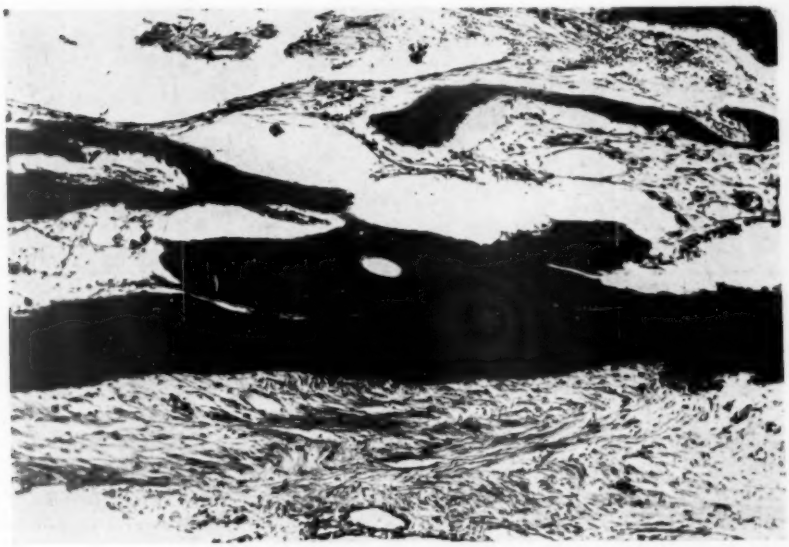

FIG. 9.—J. M. From same case as Fig. 8. Section through another portion of the graft showing new bone formation on dead bone 23 days after implantation.

or citrated blood as it was frozen while still moist and thus preserved its own fluids. Cultures from the bone were taken at the time of bottling and the only other precautions were a Kline test on the blood of the donor to rule out syphilis and a careful check of the patient's history to rule out malaria hepatitis

FIG. 10.—J. P. Man, age 28 years, with multiple war wounds of face. Operation 8–23–46. Second stage of nasal reconstruction with implantation of autogenous graft from ilium. Graft became infected and was removed two months later. Illustration shows low power view of graft. Evidence of inflammation which caused graft to be removed is shown at right end. Remainder has been revascularized and is healing.

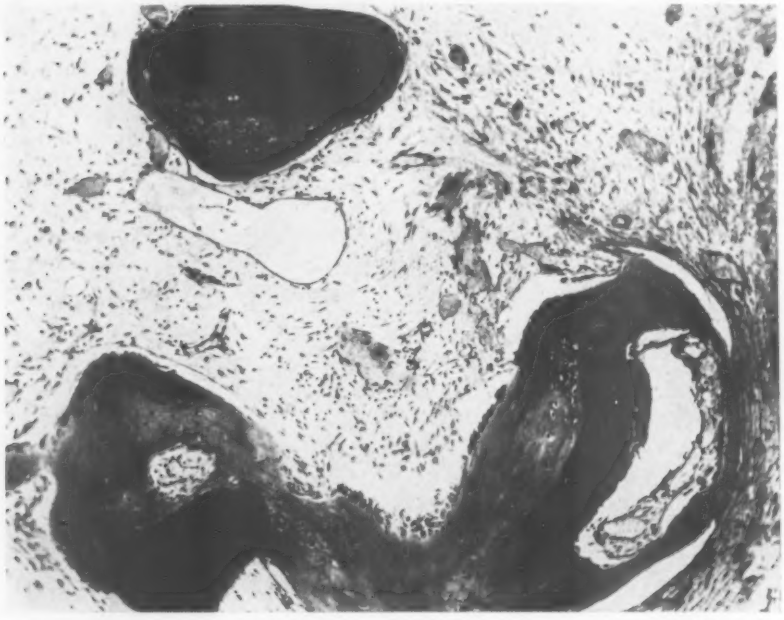

FIG. 11.—Same case as Fig. 10. High power of section through graft showing new bone forming on dead bone. The appearance is similar in all respects to that seen after grafting refrigerated bone.

or other recent acute infection. Accurate records were kept of the source of the material, the length of refrigeration and the later results after transplantation. We have constantly had in mind the need of adding to our supply of preserved bone and have sought to add to our stock by taking bone from all available sources and particularly from the iliac crest in operations upon the hip when this would not be harmful to the patients.

RESULTS OBTAINED

This preserved bone obtained from 40 different donors has been used for transplantation in 30 surgical operations upon 25 different individuals during the past year. The longest period between the time of removal of the bone and its implantation was 89 days and the shortest one day. The average period of preservation of all the bone used was 42 days. No infections or foreign body reactions occurred and in every case the wound healed by primary intention and remained healed. In no case has there been any sloughing of the preserved bone. Because all of the specimens of preserved

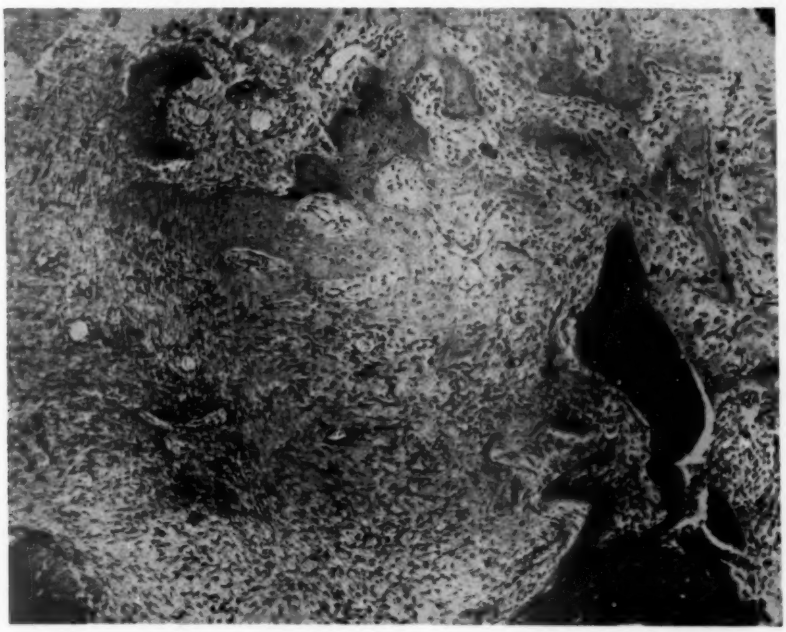

FIG. 12.—E. N. Woman, age 16 years, who had idiopathic scoliosis. Following correction a two-stage spinal fusion was done. At the first stage refrigerated bone chips were used and some of these were recovered at the second stage operation. Illustration shows section of refrigerated homologous bone chips three weeks after implantation. Osteoid tissue and new bone are seen forming on the dead bone.

bone were small it was not possible to use them in any form but that of small chips and these chips were used to pack bone cavities or to reinforce various types of fusion operations, especially of the spine. Preferably the bone should be withdrawn from the bank several hours in advance of the time it is to be used in order to allow it to thaw out but in several cases the need for its use had not been foreseen and it was necessary to use it in the frozen state. No difficulty was encountered in these cases however and it is probable that the process of preparing the fragments for use by chopping them up in small bits gave enough time for them to thaw out.

The various conditions and operations in which the bone was used are shown in the adjoining table. Of particular interest were the two cases of chronic osteomyelitis with sinuses, one at the lower end of the femur and the other at the lower end of the tibia. In both there were large cavities in the bone which it was not possible to treat by the ordinary method of extensive saucerization and skin grafting or plastic closure of skin flaps. The amount of drainage was small and of serous character. Careful débridement was done of the sinus and of the walls of the bone cavity exposing healthy bleeding bone. The cavity was washed out with saline, packed solidly with bone chips and then skin flaps were mobilized and closed. The limbs were immobilized in plaster for four weeks. Healing occurred by primary intention and the wounds have

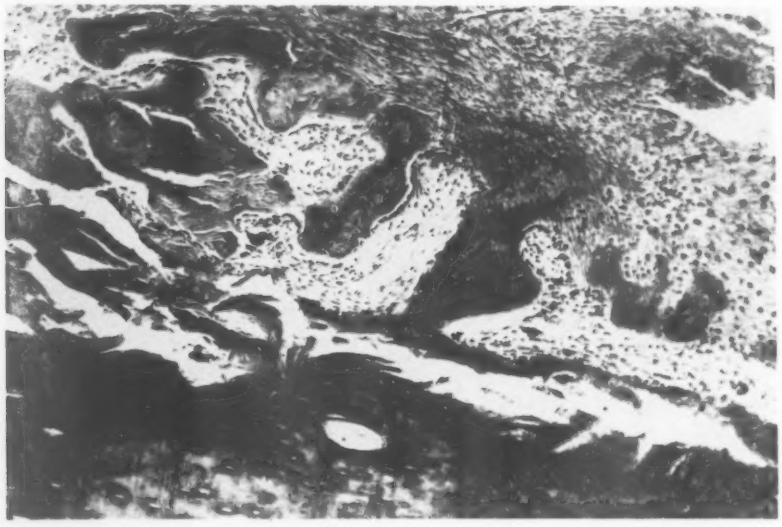

FIG. 13.—B. S. Woman, age 25, with Paralytic Scoliosis. Spinal fusion was performed in three stages. At the first operation refrigerated bone chips were implanted which were recovered at the 2nd operation 28 days later. The illustration shows a microphotograph of a section through this bone. Active new bone formation on the old dead bone may be seen. The process seems entirely similar to that seen with the use of an autogenous graft.

remained healed for follow-up periods of three and six months respectively. In one of these cases the bone used had been preserved for 90 days and in the other four days. The uneventful healing in these two cases seemed to prove the absence of any foreign body reaction of the host tissues to the preserved bone.

From a clinical standpoint the results of the use of preserved homologous bone have been entirely satisfactory. In all cases its behavior seemed to be identical to that of fresh autogenous bone. Bone cavities and defects became obliterated and the fusions became solid.

There was one failure in a case of spinal fusion for scoliosis where banked bone was used. Pseudarthrosis was discovered four months after operation.

This patient was reoperated and complete healing of the banked bone was found to have taken place everywhere except at one level where there was a line of pseudarthrosis. This area was excised and refused. Examination of the excised specimen showed the pseudarthrosis lined by cartilaginous surfaces with the adjacent bone showing all the appearance of normal healing.

THE HEALING OF REFRIGERATED BONE

Our experience with the use of refrigerated bone and that of Inclan, and of Busch and Garber who have conducted similar experiments show that from a clinical standpoint it behaves in every way similarly to fresh autogenous bone. This raises the question of how such bone acts and whether from a histologic examination of the tissues the healing is also similar.

We have recovered specimens both of fresh autogenous bone and refrigerated bone which were implanted in human spines for the purpose of promoting fusion at a varying number of weeks postoperatively. These were studied and compared with each other by Dr. Milton Helpern, Pathologist at the Hospital for Special Surgery, as well as by myself. We found no evidence that the cells in the bone transplants survived in either case. The lacunar and interosseous spaces of the bone transplants whether fresh or refrigerated were uniformly empty of living cells in the early stages of healing but there soon occurred an invasion of fibroblasts and blood vessels followed by active absorption of the dead trabeculae with large numbers of osteoclasts present. This process appeared to develop from the periphery of the transplant and then to penetrate into the interior. Three to four weeks after transplantation active new bone formation could be seen adjacent to the old trabeculae with both osteoid and osseous tissue present and many osteoblasts arranged about the latter. In other words the healing process seemed comparable in both the fresh autogenous grafts and the refrigerated bone grafts and whether the material was homologous or autogenous seemed to make no difference.

We examined sections of refrigerated bone after varying periods of preservation. The cellular tissue appeared intact and had the same staining reaction as that of fresh bone. This did not mean however that these cells were still alive any more than a normal cellular appearance or staining reaction of a piece of refrigerated steak would mean that that tissue was alive. It only indicates that the tissue is preserved in a fresh state by refrigeration. In short our views conform to those of the many other students of the function of bone transplants who have concluded that the grafts die and are then transformed into living bone by the processes of resorption and osteogenesis of the hosts tissue. In fresh grafts some cellular elements may survive but these are few and not of much importance.

We believe that the advantages of refrigerated bone lie in the fact that it is preserved in a fresh state and therefore that the processes of invasion, resorption and transformation take place more easily than with boiled or dried bone where the organic elements are dried or coagulated as pointed out by Orrell. Whether or not sterile refrigerated heterogeneous bone would serve

as well as homologous bone remains to be determined. Obviously there is a large field for further experimentation to answer this and other questions.

ORGANIZATION OF A BONE BANK

It is only one year since the establishment of a Bone Bank at the Hospital for Special Surgery but in that short time it has proved of great advantage. The method of preservation by refrigeration is simple and beyond the initial cost of a deep freeze unit of sufficient capacity, requires no large expenditure. We have experienced no great difficulty in maintaining a stock of bone sufficient for routine needs. By using this bone we have been able to save a number of patients from supplementary operations and disabilities. But thus far the bank has been organized on a small scale and has served only for the purposes of experimentation and demonstration. We have not yet attacked the real problem of obtaining and preserving large specimens of homologous bone in order that the needs of surgeons for massive grafts of every description such as may be required for the treatment of ununited fractures or defects created by the excision of tumors and other lesions may be met.

For this organization on a large scale is necessary. While amputated limbs may supply some of the need, this source is uncertain and generally unsatisfactory because of the pathologic condition which necessitates the amputation. Because of lack of knowledge of the survival period of tumor cells under refrigeration, we have not yet felt safe in using bone from limbs which had been amputated for malignant tumors. The real solution lies in obtaining bone from fresh cadavers where death has occurred from other cause than infection. The material should be removed by an operating team under sterile precautions within six hours, probably longer if the body is placed in cold storage, immediately after death.

But the obtaining of fresh bone from this source is hedged about by legal difficulties since the dead body is the property of the next of kin and the time required to obtain that person's consent may exceed the time limit within which the desired material should be removed. Even testamentary disposition of his body by a person before death, I am informed, is of no legal value without the signed approval of the next of kin.

The experience of the Manhattan Eye Bank shows, however, that many of these difficulties can be solved. By means of public education and the cooperation of many persons including physicians scattered throughout the country and the airlines, they have brought forth many donors and insured a supply of eyes which have met most of the current surgical needs for corneal transplants both in New York and other neighboring cities and have also supplied material for important research.

While the organization of a bone bank on a small scale such as the one I have described is possible and desirable in every hospital with an active bone and joint service, it seems to me that we should aim for the larger goal of supplying the needs of all surgeons requiring bone for every type of transplantation and that we should take a leaf from the book of experience of the

Manhattan Eye Bank and plan to organize a Bone Bank on a community level. In this way the cooperation of all persons both medical and lay would be obtained as the service would be available to all. It probably could subsist on a system of voluntary contributions from the recipients in the same manner as the Manhattan Eye Bank.

CONCLUSIONS

1. The preservation of fresh homologous bone material by refrigeration for later use in operations upon the bones and joints is safe and practical.

2. As nearly as can be determined both by clinical and histologic study the behavior of such bone after transplantation is similar to that of fresh autogenous bone.

3. In both cases the bone is resorbed and transformed into living bone entirely as the result of the action of the host tissues.

4. Our experience at the Hospital for Special Surgery with a bone bank organized on a small scale after one year of operation demonstrates the need for organization on a much larger scale, of a community Bone Bank to supply the needs of surgeons for bone transplants of every size and description.

DISCUSSION.—DR. W. E. GALLIE, Toronto: I have listened to Dr. Wilson's suggestion with the greatest interest, for I feel that in it there may be a contribution of much practical value.

He referred to some experimental studies which I reported nearly thirty years ago, in which it was shown that bone, either autogenous or heterogenous, when boiled and placed in intimate contact with living bone, will adhere to it, acquire a circulation through the old haversian canals, and ultimately undergo absorption and replacement as a result of invasion by living osteoblasts from the surrounding living bone. A superficial examination of such specimens might make one think there is little or no difference in the fate of boiled as compared with that of unboiled autogenous grafts. A more careful study will show, however, that in the case of the boiled grafts there are no living elements whatever, whereas in the case of autogenous grafts, although all cells in lacunae die, nevertheless those osteoblasts which lie on exposed surfaces rapidly multiply and take an active part in the creeping replacement of the graft. This is best seen in experiments where grafts are transplanted from the radius or ribs into the muscles of the back. If the grafts are not boiled they quickly become vascularized and undergo absorption and replacement with new bone, due to invasion by living osteoblasts from their own surfaces. If, on the contrary, the grafts are boiled before being imbedded in muscle, no such absorption and replacement occurs.

The outstanding difference between the autogenous unboiled graft and the boiled graft, when placed in contact with living bone, is that in the latter the process of union, revascularization and absorption and replacement are much retarded. It is because of this that when bone grafts are indicated, autogenous unboiled bone is much to be preferred.

Now, whether bone transplanted from one patient to another would retain any living elements I do not know. Our experiments on animals showed that in transplantation from one animal to the muscles of another animal of the same species, osteoblasts on the surface of the bone sometimes did live, but not always. If the animals were of a different species, no living elements survived. So it may be possible that bone obtained from one patient and transplanted into another may have the properties of autogenous grafts.

Now, whether refrigeration will destroy all the surface osteoblasts is not certain. Dr. Wilson thinks that no living cells survive the refrigeration. It would be interesting, however, to settle this question by the simple experiment of securing autogenous grafts, then refrigerating them for varying periods of time, and then transplanting them into the muscles of the same animal. This should settle whether refrigeration kills the surface cells or not.

No matter what the answer is, however, it is quite possible that bone prepared and preserved as Dr. Wilson has described, may prove to be very useful. This would be particularly the case in filling large cavities. Where the purpose of the graft operation, however, is the overcoming of nonunion or the bridging of gaps, I think the use of refrigerated bone should be supplemented by the ordinary method of using fresh autogenous bone. This limitation would, of course, be removed, if it is shown that surface cells survive refrigeration.

Dr. Wilson's suggestion is highly interesting, and is sure to stimulate renewed interest in the important subject of the transplantation of bone.

DR. PHILIP D. WILSON, New York (closing): I wish to thank the various members for their questions which I shall endeavor to answer. We did not pay any attention to blood groups in the use of material from our bone bank. Dr. Inclan laid considerable emphasis on this in his work and thought that the donors of grafts should be in the same blood group as the donee. The only thing I can say is that we experienced no reactions thus far. It is possible that if we used more massive grafts which would contain a good deal of protein material, there might be some reaction.

To the question as to whether we have experienced infectious hepatitis in any of our cases, the answer is no. In this connection, I might point out that the donor material is preserved separately and that there is no pooling of the donor material as in the case of pooled plasma. In other words, there should be no more chance of transmitting infection of this kind by the use of bank bone than by individual transfusion.

I am very grateful to Doctor Berry for his suggestion that resected portions of ribs which are frequently obtained by operations on the chest might make a convenient source of material for the bone bank.

I wish to thank Doctor Gallie for his discussion, as he has done much work on the use of homologous and heterogenous bone grafts. In looking over the work of other students on bone regeneration, I find considerable difference of opinion. Some believe that certain of the host elements in a graft survive and proliferate while others do not. There is obviously much room for further experimentation before we have all the answers, but I think that Inclan's work has proved that refrigerated bone in the form of massive grafts will work, and our own experience with the use of smaller fragments of bone certainly has been helpful in many cases and encourages us to go on and expand the method of preserving bone in a bank for general use.

PENETRATING WOUNDS OF MAJOR JOINTS*

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NEW YORK, N. Y.

EVER SINCE THE ADVENT and acceptance of the principles of asepsis, as established by Lord Lister, and the fundamental concepts of the healing of wounds put forth by Halsted, the interest of surgeons in trauma and repair has varied directly with the occurrence of war. In periods of peace a modicum of experimental and clinical work on this most basic problem in surgery continues, but with comparatively little attention by most surgeons. Rather their interest seems to be centered on the great panacea—elusive as the alchemists' dream of the conversion of base metals into gold—that will heal wounds in spite of neglect of the underlying principles of wound repair. Once Pandora's box is opened, however, and the woes of war suddenly unleashed, the problems posed by wounds become of paramount importance. Symposia are held and old truths hailed as great discoveries, and the currently fashionable wound antiseptics are exploited to their full. Yet what has been their fate, phenol, corrosive sublimate, iodine, Dakin's solution, B. I. P., the newer mercurials, the sulfonamides, and the antibiotics?

"The almost inherent urge to place some agent, with hopeful healing and anti-infective properties, in a wound seems to be deep-seated in the human breast and is as difficult to control as the better recognized human impulses. Time and experience have repeatedly demonstrated the inefficacy of such agents. Perhaps some day such an agent will be found but the search seems futile when it is realized that the key to wound infection in traumatic wounds is dead tissue, a fact which Botallo recognized almost four centuries ago, and which Lister fully appreciated."[1]

Many of the anti-infective agents are of immeasurable aid in controlling infection and extending the scope of surgery, but they are always ancillary to thorough and careful surgery. It took the British three years to recognize this in World War I and in their *Official History of the War* the development of the methods used in treating wounds of joints is divided into four phases:

1. In the early stages of the war attention was focused on incision and drainage with large tubes. With the exception of a few simple perforating wounds, suppuration was the rule with a resulting high mortality, and an amputation rate of 60 per cent for knee-joint cases with only soft part injury, and 80 per cent for those complicated by fracture.

2. Early in 1915 the treatment outlined by Colonel H. M. W. Gray was adopted. This consisted of: (1) adequate immobilization of the joint, (2) excision of infected soft parts, (3) lavage of the joint cavity after removal of

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the projectile, and (4) closure of the capsule of the joint. If suppuration was present arthrotomy was performed and drainage established only down to the joint cavity.

3. In the summer of 1916 the Carrel-Dakin method of treating wounds was adopted by the British Army and for the first time the importance of early excision of infected tissues as an essential feature in wound treatment was realized.

4. In the Spring of 1917 early and free excision of the injured area was the standard method of treatment with primary or delayed closure of the wound. This resulted in 70 per cent healing by first intention in all wounds. In joint cases only 12 per cent suppurated, while the amputation rate fell from 25 per cent to 7 per cent and the death rate from 15 per cent to 8 per cent.[2]

In World War II, notwithstanding the knowledge already available, much had to be rediscovered. The absolute necessity of wide exploratory arthrotomy and careful débridement of all wounds involving joints, was not fully appreciated at first. This was probably due to our unfamiliarity with the British experience in World War I, and with our own findings at that time, as stated in an admirable article by Pool in the *Medical Department of the United States Army in the World War*,[3] which was not published until 1927. We knew little, and that largely condemnatory, about primary resection of joints and the timing of secondary resection for suppuration. Yet these procedures had all been considered in detail by Pool.[3]

Early in 1943 the Ninth Evacuation Hospital came to the conclusion that all cases of penetrating wounds of joints should be widely opened, carefully débrided and the foreign bodies, debris and blood should be removed. Also the joint should be irrigated with saline, and the capsule closed. The closure of the capsule was thought to be so important, that if a gap existed a sliding flap of skin or fascia was employed.

Complete immobilization of the joint was of paramount importance and in the case of a knee joint this was accomplished by means of a hip spica. The delayed primary suture of the soft parts was performed four to seven days later. When penicillin became available this was placed in the joint in the dosage of 10,000 units at the conclusion of operation. It was repeated at 24–48 hour intervals thereafter for two or three doses, and the patient was also placed on systemic penicillin.[4]

At about the same time, this hospital unit, which was functioning near Naples, admitted a group of French soldiers with well-established suppurative arthritis of the knee. A lower thigh amputation was necessary as a life saving measure in one instance and it appeared that this would be required in five other cases. At the suggestion of Colonel Etienne Curtillet, the French surgical consultant, five resections of the joint were performed. This seemingly radical procedure had been advocated 75 years ago by Ollier.[5] The sepsis subsided and healing was prompt in all five cases, only one case failed to develop solid fusion.[6] These conceptions of treatment were immediately extended to all the hospitals in the Naples area by the teaching and work of Lieutenant Colonel Oscar Hampton and Major Champ Lyons with the cooperation of the various

orthopedists,[7] and further, the principle of re-débridement in the presence of sepsis was established by them.[14]

As a result of this early experience a detailed description of the treatment of penetrating wounds of joints was included in Circular Letter Number 2 of the Surgeon of the Seventh Army just prior to the Southern France Campaign.[8] The response was more than gratifying and reports came from both the forward and base installations that these wounds healed cleanly when so treated and the only ones that became septic were those that had been neglected or in which débridement was inadequate, usually by new and inexperienced surgeons. Two of the Evacuation hospitals reported their results of arthrotomy and débridement of penetrating wounds of the knee joint in detail. Of the 227 cases treated by them, two were suppurating at the time of the initial débridement—one 10 and the other 14 days old. None of the others showed any signs of infection when evacuated to the rear three to seven days after debridement. There were no amputations in this group.[9]

In the ancient and modern history of military surgery, there has accumulated enough experience in the treatment of knee-joint wounds to give us confidence that our problem, to a limited extent, is solved. We now realize that if these wounds are given the proper primary treatment, suppuration will rarely develop.

The same happy outlook cannot be said to apply to wounds of the hip joint. There has always been considerable difficulty in obtaining accurate statistics on the incidence of wounds of this joint. The proximity of the hip to the femoral and iliac artery, as well as to the bladder and rectum, makes it likely that in many instances death supervenes promptly. This may account for the fact that compound penetrating wounds of the hip-joint were not as common a finding in the forward Army hospitals, as were the knee-joint wounds. On the other hand it is safe to assume that a projectile may produce tears of the capsule of the hip-joint, or lesser fractures of the head and neck of the femur, and still remain undetected as hip-joint injuries.

Regardless of the number of compounded wounds of this joint that are seen in either war or in civilian practice, they are likely to be tragic when they occur.

We have been unable to find any worthwhile contributions to the literature on this subject since the published work of Lagenbeck[10] and Otis[11] 75 years ago. Lagenbeck had collected 132 cases during the Franco-Prussian war, and had seen or treated most of them. He speaks of three forms of treatment:—the conservative, resection of the head of femur and disarticulation of the hip. His conservative treatment was definitely the most effective. There were 88 cases in this group, 63 proved fatal. A mortality rate of 71 per cent! Resection of the head of femur was attended by a mortality of 83.9 per cent, while disarticulation at the hip joint as a mode of treatment caused death in each instance.

A review of his cases in the conservative group leaves the impression that his treatment consisted in the main of probing the wound, immobilization and

hot poultices. There is no mention of débridement as we know it today, and no wide exposure of the joint.

Many of his recorded cases were not suspected of having hip-joint involvement during the early period after injury. They were transported to distant hospitals, and it was only after the manifestations of suppuration became obvious that the diagnosis was made. In spite of his figures he favored primary resection of the head of the femur before suppuration had a chance to develop. His belief was that under these circumstances the mortality rate would be lower than in the conservative group.

Otis was very sanguine on the subject of hip-joint wounds in general. He hardly saw a case of recovery of a gun-shot fracture of the hip-joint by expectant treatment, which did not leave a doubt in his mind in regard to the correctness of diagnosis. (This was of course before the days of x-ray.) He arrived in consequence at the conclusion that the expectant treatment must be rejected in all cases, as soon as the nature of injury to the hip-joint became evident. He also favored resection of the head of the femur as the treatment of choice.

In the British medical history of World War I[2] there was an estimated mortality of 60 per cent for all wounds of the hip-joints. Débridement, closure of the joint capsule, and removal of the femoral head if badly comminuted, were advised[12] as the primary treatment. Where sepsis was already established the head was excised routinely and wide drainage obtained. If excision failed, the leg was amputated through the hip-joint. The end results in all cases who survived without amputation were poor, with a grave loss of function and severe crippling.

The medical history of the U. S. Army in World War I[3] devoted little or no attention to its experience with hip-joint wounds, other than to point out their serious nature. The very lack of comment implied an inability to answer the problem. In contrast, the treatment of knee-joint wounds was clearly detailed, and today serves as a model. Any improvement in results, in the treatment of knee-joint wounds in World War II must be credited to the general advances in the surgical adjuvants, and not to changes in the underlying surgical principles.

It became evident to one of us (F. B. B.), as Surgical Consultant of the Seventh Army in France, that the surgical principles which were being so successfully applied to knee-joint injuries, were being ignored in wounds of the hip. Unlike the knee, a thorough exploration and debridement of a hip-joint is a formidable procedure in a severely wounded patient. And yet, if the principle of debridement is valid for the knee, all the more reason it should be applied to the hip with its deep location, its many adjacent muscle bellies and planes, all favoring the development of infection.

It had been observed that on the rare occasion when a hip-joint was explored it was through enlargements of the wound of exit or entrance, which naturally gave a limited exposure to the entire joint. Unlike the knee, the hip is so deeply placed that a simple anterior, lateral or posterior incision will not

lay bare all its secrets. The operator could not end his procedure with the sense of satisfaction that all devitalized muscle had been excised, and that the area had been thoroughly cleansed and freed of all foreign debris.

If he glimpsed the capsule of the joint it was at the bottom of a deep hole, and only a limited portion was in his field of vision. The intricate pattern of overlying muscles does not lend itself to bold incisions, which require only an inch or two more in length to get a good look at the pathology. Boldness of this sort would result in damage that in turn might produce ischemia, or paralysis and atrophy to muscle groups.

In March, 1944, several Evacuation Hospital surgeons in the Seventh Army were requested to perform arthrotomies on all suspected penetrating hip-joint wounds. The operation was to be performed initially, or within a 72-hour period, whenever the condition of the patient permitted. The arthrotomy was to be a formal procedure which would give wide exposure to the joint. Considerable thought was devoted to the type of incision which would give the best exposure, and yet avoid being too destructive. It was agreed that the Smith-Peterson incision was best suited for this purpose, and that if the posterior and inferior portions of the joint needed attention that the Langenbeck or Kocher incisions could be employed separately or in addition. The wounds of entrance or exit were to be incorporated in the incision if convenient, and otherwise they were to be debrided individually.

In April, 1945, one of us (J. E. T.) had his first opportunity to put this plan into effect. The first case was most convincing in two respects. First, that the Smith-Peterson incision gave excellent exposure of the anterior and superior aspects of the joint, and that palpation of the remainder of the capsule would determine the need of an additional posterior incision. Second, the extensive deep destruction to the gluteal muscles could never have been properly débrided by means of any other incision. An infection developing in this situation would have extended directly into the opened joint.

Within a four-week period leading up to the end of the hostilities in Europe, we operated on nine hip-joint wounds. Seven of the nine cases had penetration of the joint capsule, and the remaining two had contusions of the capsule without frank penetration. Contusion of the capsule was considered by Langenbeck[10] to have serious potentialities.

Six of the patients were American soldiers, and three were German prisoners of war. (We have a limited follow-up on all the Americans which has been added to the case reports. No information on the Germans has been obtainable.)

In six cases the typical Smith-Peterson approach was used, and in one a modification of it sufficed. In this latter case it was only necessary to lengthen the wound of entrance on the antero-lateral aspect of thigh, up to the anterior superior iliac spine, and then for an inch along the crest, only detaching the tensor fascia muscle. In two cases the Langenbeck incision was employed.

The nature of the Smith-Peterson incision demanded that its horizontal portion be closed in all layers. The tension was so great on the re-sutured

gluteus medius muscle, that the overlying skin was closed to give it additional support. The remainder of the wound was left wide open, with the expectation that a secondary closure would be performed within a week at some hospital in the rear.

Drainage was used in only one case, the drain was brought out through a posterior stab wound, splitting the gluteus maximus muscle in the line of its fibers.

Dry, fine mesh gauze was used as a dressing over the raw wounds, and in each instance a hip spica was applied. Every case, when possible, was evacuated to the rear within a 48-hour period. The purpose of early evacuation was to have the patient in a permanent installation, in the event suppuration developed.

FIG. 1-A.—An x-ray of pelvis in Case 1, taken 21 months after injury. The slight upward shift of left half of pelvis can be seen.

All of the patients in the following case reports were admitted to the 9th Evacuation Hospital while it was functioning in Germany during April and May of 1945.

CASE REPORTS

AMERICAN SOLDIERS

Case 1.—J. E. K. This patient received a perforating rifle wound at 11 A.M. on April 3, 1945. Admitted on April 3, 1945. The wound of entrance was in the left inguinal region and the wound of exit in the left buttock. The abdomen was soft and there was no evidence of rectal injury or injury to the femoral vessels. X-ray revealed an extensive comminuted fracture of the left ilium involving the acetabulum.

The patient was treated for shock. He was brought to operation at 3:45 P.M., April 4, 1945, almost 29 hours after injury. Pulse 100. Operator J. E. T.

Pathology. The wound of entrance was just medial to the anterior superior iliac spine. The bullet had entered the abdominal wall and had passed extra-peritoneally to pierce the ilium, shattering it into one large fragment and several smaller ones. It traversed the superior lip of acetabulum in its path, unroofing the joint. In emerging from the ilium it destroyed the gluteus minimus and maximus over a diameter of about 3 inches, leaving a large defect. The superior gluteal vessels had been completely divided. There were many small loose bone fragments, but no debris, just old blood clots.

FIG. 1-B.—A spot film of left hip in Case 1. The hip-joint shows extensive arthritic changes and is painful, but there is 25 degrees of flexion.

Procedure. Using a Smith-Peterson incision, the antero-superior aspect of the joint was exposed. The above pathology was outlined. The capsule of the joint was opened by means of a "Y"-shaped incision. The head of femur was examined and found to be uninjured. The joint was then thoroughly irrigated with warm saline, and closed with interrupted chromic gut sutures. The defect in the joint where the superior lip of the acetabulum had been destroyed, could not be closed by a muscle flap of gluteus minimus. This muscle was completely lacking in blood supply and had to be removed in its major part. The severed superior gluteal vessels were ligated. The wound was thoroughly

irrigated and 10,000 units of penicillin were instilled into the hip joint. Closure was performed by re-attaching the gluteus medius to the iliac crest, and suturing the overlying skin with interrupted fine wire sutures. The vertical portion of the Smith-Peterson incision was not sutured.

The wound of entrance was incised down to fascia, and a local debridement was performed. The wound of exit was located in the left buttock four inches from the midline and on a level with the greater sciatic notch. It was enlarged laterally revealing a large defect of gluteus maximus that communicated directly with the space left by excising the gluteus minimus muscle. It was impossible to obliterate the cavity. The wounds were left open, dry fine mesh gauze was applied to the raw surfaces. No drains. A plaster hip spica was applied.

Follow-up. Secondary closure was performed in England, in April 1945. He was evacuated to the United States on June 1, 1945, with his wounds healed and in a double hip spica which was removed during June 1945. He wore a brace and was ambulatory from July 1, 1945. The brace was discarded in February 1946. He was discharged from the Army on December 10, 1946.

He was examined by one of us (J. E. T.) on January 16, 1947. He is now gainfully employed at a desk job. His main complaints are pain in the hip, and to a less extent pain in the left knee and left flank. He uses a cane and walks with a definite limp.

On examination all his wounds are found to be cleanly healed. There is ¾" measured shortening on the left side, in measuring from the umbilicus to the medial malleolus. When measuring from the anterior superior iliac spine the left leg measures the same as the right. The shortening is due to the upward shift of the fractured ilium and acetabulum.

The motion at the hip is limited to 20 degrees flexion, 5 degrees extension, 5 degrees internal rotation, and 5 degrees external rotation. The extension at the knee-joint is complete, and he can flex the knee to 90 degrees. There was marked atrophy of the left thigh and left buttock, there was only slight atrophy of the left calf.

X-ray examination of the pelvis to include the left hip reveals extensive healed comminuted fractures of the left ilium which involves the acetabulum. Definite encroachment on the pelvis is shown by the medially displaced acetabulum and pubic fragments. There is upward displacement of the acetabulum, plus cartilage absorption of the articulating surface of both the head of the femur and the acetabulum (Fig. 1).

Comment—This case illustrates a very severe type of penetrating wound of the left thigh, where a comminuted fracture of the ilium communicated with the hip-joint. The damage to the gluteal muscles was extensive, including early ischemic necrosis of the gluteus minimus due to destruction of its blood supply. Debridement of this wound could never have been accomplished as easily or as completely through any other type of incision. It is felt that if this patient had been given the usual conservative treatment with wound debridements, he would have been an excellent candidate for deep wound infection and secondary suppurative arthritis.

Functionally his result is poor, and he may come to hip fusion to control pain. On the basis of World War I experience he may well have been included in the 60 per cent mortality group.

Case 2.—H. H. S. The patient received a bullet wound of left upper thigh on April 9, 1945. He was admitted six hours later. X-rays revealed a comminuted fracture of the neck of femur and greater trochanter. He came to operation 22½ hours after injury. Operator J. E. T.

Pathology—The wound of entrance was situated on the antero-lateral aspect of middle third of left thigh. In coursing upwards the bullet traversed the base of the neck of left

femur to lie, finally, just beneath the skin of left buttock about three inches lateral to the anus. The greater trochanter was also comminuted. In its course it destroyed about two-thirds of the tensor fascia muscle, and locally destroyed portions of the deep surface of the gluteus maximus muscle. The fracture lines extended into the joint proper.

Procedure—Smith-Peterson incision employed with the wound of entrance included in the vertical portion of the incision. The devitalized tensor muscle and the destroyed portions of the gluteal muscles were excised. Some clothing and bits of steel jacket from the bullet were also removed. The capsule of the joint was opened through a Y-shaped incision on its anterosuperior aspect and the fracture was seen to communicate with the joint. Actually the bullet had traversed the trochanter at an extra-capsular point.

The joint was irrigated with warm saline, and the capsule closed with a lock stitch of continuous chromic gut. 10,000 units of penicillin were injected into the joint. The bullet was then excised from beneath the skin of the buttock.

A postero-lateral incision, splitting the fibers of gluteus maximus, was made, and a rubber tube drain inserted to a point just posterior to the fracture line. (To be removed in three days.)

The Smith-Peterson incision was closed in layers, except for the distal half of its vertical portion.

The hip was reduced by the Ledbetter maneuver and a plaster hip spica was applied.

Follow-up.—A letter received from patient on December 8, 1946, is as follows:

> "I received your letter asking me about my hip wound. Well it sure turned out better than I ever thought it would. You asked me a few questions in your letter, I'll do my best to answer them.
>
> "The first thing, my hip is healed and well. After I was operated on in the 112 Gen'l, I was put in traction. Ten days after they operated, the wound was well healed, but the bone itself would not knit. I was in traction 10 weeks and sent back to the States, here I was put in skin traction for three weeks, then up on a full leg brace, which wasn't so good. I was sent to Percy Jones Hospital after that, oh yes, this brace was gotten at Winter Gen'l Hopital in Kansas. After one month at Percy Jones they operated again and put in a steel plate which turned out all right so far.
>
> "As for working I haven't done anything yet. I tried a few things back here on my Dad's farm but that's out. My leg is an inch short and throws me off balance to carry anything. So I have to look for some other sort of a job. My knee has only 90 degree bend and hip partially stiff.
>
> "I am home now on Terminal leave, which is up the 15th of December, far as disability pension I wouldn't know as yet."

Comment.—This case illustrates a bullet wound causing a severe compound fracture of the greater trochanter of femur, and the fracture line extending into the joint. The deep-seated destruction of muscle, and the clothing carried into the depths of the wound would have been difficult to discover with a simple type of incision. Suppuration of the hip joint would have been a likely complication following the conservative form of treatment.

Case 3.—D. P. This patient received a shell fragment wound of the upper left thigh on April 19, 1945. He was admitted and operated on the same day. Operator: J. E. T.

Pathology.—X-ray had shown two large shell fragments adjoining the hip, one of which looked as though it might have penetrated the capsule. Actually one fragment was found lying on the antero-superior aspect of the capsule but had not penetrated it. The other one was found medially beneath the sartorius muscle.

Treatment.—Smith-Peterson incision. The shell fragments were removed and the destroyed muscle tissue debrided. The joint capsule was not opened. The Smith-Peterson incision was closed except for the distal half of its vertical portion. A hip spica was applied.

Follow-up.—A letter received from the patient's father on Dec. 5, 1946, states that the patient underwent no further surgery. He was discharged from the Army and is now attending school. His hip is said to have 20 per cent limitation of motion.

Comment.—This case was subjected to more surgery than was needed. The capsule of the joint was contused and not penetrated. It is inevitable that a certain per cent of negative explorations will occur.

Case 4.—T. A. M. This patient received a bullet wound of the right anterior thigh on April 23, 1945, at 5:30 A.M. *Primary operation* on April 24, 1945, at 2:30 A.M. 21 hours after injury. Operator: C. F. Stewart.

Pathology.—A simple debridement of the wound of entrance was made and the tract was explored. The entrance was just lateral to the femoral vessels on the anterior thigh, and an x-ray had shown the bullet at the level of the neck of femur. It was thought that it was lying anterior to the capsule just below the sartorius muscle. A vertical counter incision was made between the sartorius and the tensor fascia muscles. At the end of two hours of search the procedure was abandoned. The wounds were left open and dry dressings were applied.

Course.—On April 25, 1945, check-up x-rays, which included a lateral view, suggested that the bullet had penetrated the joint capsule, and was lying against the neck of femur.

Secondary Operation on April 25, 1945, at 3 P.M. Operators: C. F. Stewart and J. E. Thompson. The original counter-incision was extended upwards and converted into a Smith-Peterson approach. The antero-superior aspect of the joint was exposed. The capsule was opened with a V incision on its anterior surface, and the joint filled with 5 to 10 cc. of bloody fluid. On the anterior surface of the head was a minor crushing injury to the cartilage, not sufficient to require débridement. The bullet was then found embedded within the substance of Bigelow's ligament opposite the superior surface of the femoral neck. It was partially within the joint. The bullet was removed and the openings in the capsule were closed with a continuous lock-stitch of chromic gut after irrigating the joint with warm saline. 10,000 units of penicillin were instilled into the joint.

The wound was then closed in layers except for the vertical portion of the Smith-Peterson incision which was not sutured. A hip-spica was applied.

Follow-up.—A letter was received from this patient on Jan. 15, 1947. He was still in the army as of that date. He states that his only subsequent operation was for secondary closure of his wounds. He is now suffering from slight stiffness at his hip-joint, with occasional pain in the hip and back.

Comment.—This case beautifully illustrates the problems of penetrating hip-joint wounds as encountered and treated in the past. It emphasizes the time consumed in trying to trace the path of a foreign body which has penetrated deep into the tissues around the hip-joint. It shows the inadequacy of using an ordinary debridement incision to give the proper exposure. The knowledge gained by the preceding cases was of great help in deciding that a secondary operation was necessary, particularly after the x-rays were reviewed and new ones were obtained.

Case 5.—S. D. S. This patient received a bullet wound of the left thigh on April 24, 1945, at 11:45 P.M. The wound of entrance was on the antero-lateral aspect of the left thigh in the upper third. X-ray showed a fragmented bullet which seemed to be in the hip-joint.

Operation was performed on April 25, 1945. Operators: G. Crawford, J. E. Thompson.

It was decided to approach this case using only the vertical portion of the Smith-Peterson incision, as the bullet was seen by x-ray at a point just anterior and inferior to the neck of femur. The incision was made to pass through the wound of entrance, and extended deeply between the sartorius and rectus femoris on the medial side and the tensor muscle laterally. The capsule of the joint was exposed and incised in the line of its fibers. The bullet fragments were removed both from the capsule and curetted from the substance of the neck of femur.

The joint was irrigated with warm saline, and snugly closed. 10,000 units of penicillin were instilled into the joint. The upper half of the incision was closed and the remainder left open. A hip spica was applied.

Follow-up.—A letter from the patient on December 12, 1946, stated that his wound was sensitive but completely healed. He has occasional pain and stiffness of the hip-joint, particularly when he walks or stands too much. Upon his discharge from the Army he was allowed 30 per cent disability. He now has an easy civil service job.

Comment.—The exposure using this type of incision was quite difficult in that it required considerable heavy retraction and only a limited view of the anterior part of the capsule. The many arterial branches entering the tensor muscle in its distal half added to the difficulty. The operation would have been easier, and the exposure improved by detaching the origin of the tensor muscle from the anterior superior spine and the infra-spinous portion of the crest of the ileum. This modification of the Smith-Peterson incision would be perfectly adequate to approach the antero-inferior portion of the hip-joint.

Case 6.—N. M. This patient received a bullet wound of the left buttock on May 4, 1945, at 9:30 P.M. and was admitted on May 5, 1945. X-ray revealed the bullet adjoining the neck of femur on its posterior aspect. Operation at 5 A.M. on May 6, 1945, 32 hours after injury. Operator: G. Crawford.

A posterior approach was utilized as described by Langenbeck, passing through the wound of entrance. The fibers of the gluteus maximus were split, and the gluteus medius retracted anteriorly. The bullet passed through the pyriformis muscle to enter the joint. The capsule was incised and the bullet removed. A small fractured area of the rim of the head of femur was debrided and the joint was irrigated with warm saline. The capsule was closed and 10,000 units of penicillin were instilled into the joint.

The soft tissues were not sutured. A hip spica was applied.

Follow-up.—The only information that could be obtained about this patient was that he was back at regular duties with the Army of Occupation in Europe in February, 1946. This fact would indicate that his disability was minimal.

Comment.—This case illustrates the adequacy of the posterior approach for selected cases where the pathology is limited to the posterior aspect of the joint. It is a much less destructive incision.

German Prisoners

(No Follow-Up Obtainable)

Case 7.—E. S. The patient received a perforating bullet wound of left thigh at 4 P.M. April 5, 1945. He was admitted at 1 A.M. April 6, 1945. Examination revealed a wound of entrance just below and medial to the left anterior superior iliac spine, the wound of exit was in mid-left buttock. There were other irrelevant wounds. The clinical signs pointed definitely to joint involvement.

Operation.—April 6, 1945, at 2:20 P.M. 22½ hours after injury. Operator: J. E. T.

Pathology.—The bullet had traversed the thigh and buttock just superior to the capsule. No penetration of the capsule could be found. The gluteal muscles were quite healthy looking and only a moderate amount of debridement was necessary.

Procedure.—Smith-Peterson incision. The capsule was opened with a V-incision, the joint was inspected and found to be negative. Several small fragments from the bullet were removed from the soft tissues outside the capsule. The capsule was snugly closed with a running lockstitch of chromic gut. Penicillin 5000 units were instilled in the joint. The incision was closed in layers except around the wounds of entrance and exit. A hip spica was applied.

Comment.—This case had no actual penetration of the hip-joint in spite of the clinical signs, which were probably due to contusion of the capsule. There was very little deep destruction of soft tissues, so that the end result will not be materially benefitted by the Smith-Peterson incision.

Case 8.—K. G. The patient was admitted on April 11, 1945, with a penetrating bullet wound of the left buttock. An A. P. x-ray view was taken and the bullet was interpreted as lying in the soft tissues of the buttock.

Operation.—April 11, 1945. Operators: K. E. Black and T. Healy.

First Procedure.—A transverse incision was made through the wound of entrance in the line of left buttock crease. Considerable time was spent in an unsuccessful effort to find the bullet; only a gutter fracture in the outer table of ileum was discovered. Further operation was abandoned.

Postoperative x-rays were taken on April 12th and 13th. A lateral view taken on the latter date gave fairly definite evidence that the bullet was imbedded either in the capsule or in the joint itself.

Second Procedure.—April 13, 1945. Operators: J. E. Thompson and K. E. Black.

Procedure.—Smith-Peterson incision. The anterior and superior surfaces of the capsule showed no evidence of penetration or trauma. The bullet could not be seen or felt. A bi-manual examination with a finger in each of the anterior operative and posterior wound of entrance revealed that the bullet, after creasing the outer table of ilium, had entered the base of acetabulum at about 7 o'clock (in the recumbent position).

The capsule of the joint was incised from the base of neck to acetabular rim along its superior surface, and then converted into a Y by an additional incision posteriorly inclined to get sufficient exposure. The base of the bullet was exposed, lying partly in capsule and partly in the joint. It was separated and cushioned from the femoral head by the "Labrum Glenoidal," in whose substance it was also imbedded, and which it had partially divided at one point along its periphery. The bullet was removed and two small clots evacuated, no further evidence of joint damage could be detected.

The capsule was closed with a continuous lock-stitch of chromic gut. The Smith-Peterson incision was completely closed in layers, relying on the posterior wound for drainage. A hip spica was applied.

Comment.—This case illustrates joint involvement can be missed, particularly where x-rays are misinterpreted or the views are not satisfactory. The Smith-Peterson incision distinctly facilitated the location and removal of the bullet. Suppuration would very likely have developed, as one of the complications, if conservative treatment had been followed:

Case 9.—L. N. The patient was admitted at 3:20 A.M. on April 23, 1945, with a gun shot wound of the buttock. X-ray examination showed the bullet lying within the neck of femur at the level of the capsule attachment near the posterior cortex.

Operation.—April 23, 1945. Operators: G. Crawford and J. E. Thompson.

Pathology.—The bullet entered the left lower buttock 8 cm. from the midline, and pierced the hip joint through the superior gemellus 1 cm. lateral to the rim of the glenoid. It penetrated the head of the femur through a small round hole and passed down the neck of femur just beneath the cortex.

Procedure.—Incision was the postero-lateral approach of Langenbeck. The gluteus maximus tendon was partially incised near the trochanter and the incision extended toward the postero-superior iliac spine splitting the muscle fibers. The origin of gluteus medius was slightly freed from the trochanter and the muscle retracted anteriorly. The joint capsule was exposed and opened inferior to the pyriformis muscle. It was opened with a right-angled incision. The bullet was removed by unroofing the tunnel in the head and neck of femur.

The joint was lavaged with warm saline, and closed with a continuous lockstitch of chromic gut. 10,000 units of penicillin were placed in the joint. The exploratory wound was closed in layers. The wound of entrance was debrided and left wide open. A plaster hip spica was applied.

Comment.—This posterior approach of Langenbeck gave beautiful exposure after the origin of gluteus medius was partially detached. The best exposure of the head was obtained posterior to the pyriformis, instead of anterior to it as described by Langenbeck.

SUMMARY

A penetrating wound of a joint, aside from its destructive effect on the joint mechanism, is likely to result in suppuration unless the utmost care is exerted towards its prevention. This sequence of events occurs in any joint, large or small and seems to have a direct bearing on the delicate blood supply to the cartilaginous surfaces of the joint. A wound that combines the destruction of cartilage with the introduction of foreign debris is even more likely to develop this unfortunate complication.

Suppuration involving the hip or knee-joint at times is attended with such severe sepsis that life is threatened. The same threat to life is rarely seen following suppuration of the other major joints such as the shoulder, elbow, wrist and ankle, but the same principles of prevention and treatment of these joint wounds should be followed.

Warfare presents the opportunity to see joint wounds in sufficient numbers and variety to permit an organized surgical attack on the problem, in an effort to reduce the morbidity and mortality.

TABLE I

PENETRATING WOUNDS OF KNEE-JOINTS

Source	Era	Number of Cases	Suppuration	Amputation	Mortality
British Army	1914	?	Nearly all cases	60–80%	?
	1916	?	25%		15%
	1917	?	12%	7%	8%
U. S. Army (Pool)	1918	34	8.8%	?	?
U. S. Army (two evac. hosps.)	1945	227	0.9%*	0	0

* These two cases were suppurating on arrival at the hospital. One injured 10 and the other 14 days prior to admission.

A glance at Table I reveals that in 1917 the mortality rate following knee-joint injuries had dropped to 8 per cent as reported by the British Army; while in 1918 the incidence of suppuration as reported by the U. S. Army Medical Dept. was 8.8 per cent.

Pool outlined in detail the treatment of penetrating wounds of the knee joint from his experience in World War I, and today it serves as a model. The principles of treatment which he advocated were employed by several Evacuation Hospitals in the U. S. Seventh Army during 1945. In reporting 227 penetrating knee-joint wounds, it is to be noted that only two cases developed suppuration. Although the follow-up is incomplete, none are known to have died or to have required amputation. In brief, the underlying principles of treatment are as follows: (1) Wide formal arthrotomy through the wound of entrance or exit if convenient, but the essential point is good exposure of the inside of the joint so that all devitalized bone and cartilage, debris and foreign bodies can be removed. (2) Copious irrigation of the joint with warm saline. (3) Separate debridement of the wound of entrance and exit. (4) Complete, water-tight closure of the joint capsule at all points. Where a defect of capsule exists, it must be closed by a sliding flap of skin or fascia, or even a free fascial graft if necessary. (5) The skin is left open to be closed secondarily on the 4th to 7th postoperative day. (6) If a compound fracture of the patella exists, the patella in most instances should be excised. (7) The only addition to the treatment as formerly outlined by Pool, was the local and systemic use of penicillin, and the emphasis on complete postoperative immobilization of the knee-joint by means of a hip spica instead of a high thigh cast.

TABLE II

PENETRATING WOUNDS OF THE HIP JOINT

Source	Era	Number of Cases	Number of Cases Followed	Total Mortality
Langenbeck (Franco-Prussian War)	1870–71	132	131	77.2%
Otis (Civil War)	1865	386		85%
British Army (World War I)	1914–18	?		60%
Madier (French Army)	1914–18	39	37	37%

A glance at Table II shows the high mortality attending hip joint wounds as seen in previous wars.

In World War II, hip-joint injuries continued to be a serious problem with appreciable numbers suppurating and developing profound sepsis. It became apparent that the surgical principles which had been applied so successfully to knee-joints were not being carried out for the hip. Its deep location made it difficult to approach, debridements were as a result usually incomplete, and inspection of the joint capsule was inevitably rare. In addition minimal injuries to the capsule; head, neck and femoral trochanter were often overlooked early after injury, because one's attention was not specifically focused on the joint itself.

In March 1945 it was suggested by the 7th Army Consultant that all suspected hip-joint wounds were to be submitted to a formal arthrotomy. The Smith-Peterson approach was to be used by preference; and where it was desirable to expose the joint posteriorly, the postero-lateral approach of Langenbeck was to be employed.

We encountered nine penetrating hip-joint wounds during the month of April 1945. The pathologic findings were as follows:

a. Fractures involving ilium and acetabulum ..... 2 cases
b. Fracture of the neck and greater trochanter of femur 1 case
c. The capsule penetrated and the bullet found imbedded in capsule and partly within joint, with minimal damage to the head or neck of femur ..... 3 cases
d. Bullet lying completely imbedded in the neck of femur 1 case
e. Simple contusion of the joint capsule ..... 2 cases

Six cases were American soldiers, and three were German prisoners of war. No follow-up has been obtainable on the Germans, but letters have recently been received from all the Americans. None of the six cases suppurated, none had to be amputated and there were no deaths. None have draining sinuses, the wounds being completely healed. Five out of the six complain of some pain and have some degree of limitation of motion. One of the most severe cases was personally seen and examined, he walks with a marked limp, has a moderate amount of pain and only about 25 per cent motion at the hip joint. X-ray examination shows an upward shift of acetabulum secondary to mal-union of a comminuted fracture of the ileum. There is also marked arthritic change about the joint (Fig. 1).

CONCLUSIONS

In conclusion it is thought that the complications of penetrating joint wounds will be reduced to a minimum by adhering to the following principles of treatment:

1. Operation at the earliest possible moment after injury.
2. Wide exposure of the joint, by means of a formal arthrotomy, in order that the capsule and inside of the joint can be thoroughly inspected.
3. The joint should be irrigated with saline and completely cleansed of all devitalized bone, cartilage and foreign debris.
4. The joint capsule must be closed "water-tight" at all points.
5. Complete immobilization of the joint postoperatively.
6. Penicillin locally and systemically.

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DISCUSSION.—DR. FRANK B. BERRY, New York: Six cases is not a large series, but I think six cases of wounds such as you saw in the last patient, all of which are thoroughly healed without having undergone sepsis, are noteworthy in wounds of the pelvis and hip joint. I think this principle of debridement can be applied to civilian life. More than 20 years ago when I was a junior on the staff, I opened a knee joint for a bullet wound with compound fracture, as described by Doctor Thompson, debrided it and sewed it up tight. Twelve days later the patient had complete mobility of the joint. I was impressed with this.

Doctor Pool, who was with us, had a reprint of his father's to guide us, and when we were confronted with these cases we early established the principle of opening and debriding all wounds of the knee joint. I talked it over with Doctors Taylor and Thompson, who are here, and with Doctor McNeil of the Sacramento Unit, and we decided that up to three days, if we were not able to do it at first, we would similarly perform formal arthrotomies in hip joint wounds, realizing that in wounds involving joints, if suppuration does not result immediately, there are certain natural defenses. Hence, during the latter part of the war we elected to try this procedure. Instead of sending patients back to face a period of sepsis, we sent them back with clean, even though damaged joints, which could be handled by the orthopedists in general hospitals, who could then proceed with these patients who were not septic.

When we were in Naples we were detached from the American Army and assigned to the French. This gave us six months to follow and study our patients as we were not obliged to evacuate our severely wounded. We were confronted with six patients with suppurating knee joints. We went around to our American friends but could not get any help on how to handle them, except to immobilize and amputate when necessary. We did have to amputate in one instance to save life. The French surgeons said, why not resect these joints? Inasmuch as the French did not supply prostheses, we were confronted with the necessity of choosing between amputees without prostheses, or joint resection and stiff leg, so we elected to resect these patients.

(Slides) This boy was resected and sent back with his wound healed, with the thought that at least the leg was preserved, and that some future operation could be performed to strengthen the leg. We were confronted with these two problems, so we went back to resection as advocated many years ago, and considered it a worthwhile procedure and preferable to amputation.

DR. GUY A. CALDWELL, New Orleans: This is a very excellent lesson in technic, worked out in military life, which should be carried into civilian life. Many small puncture wounds of the knee which look harmless at the time, too often result in joint suppuration, even when penicillin has been administered. Such wounds need exactly the same management that has been outlined by the speaker, viz., debridement, cleansing the joint, suture, immobilization and penicillin therapy.

DR. I. RIDGEWAY TRIMBLE, Baltimore: The nature of residual pain is most interesting. I should like to ask if the incidence of causalgia was studied. A young man wounded in 1944 came under my care recently. He was struck in the ankle, with partial severance of the posterior tibial nerve, and was in the hospital for 19 months. He had so much pain that he came to the orthopedic surgeon for amputation. If he stubbed his toe he would cry with pain; scuffing his foot gave intense pain. He was submitted to a lumbar sympatectomy and has since been completely relieved of pain.

MAJOR GENERAL NORMAN T. KIRK, Washington, D. C.: We should thank Doctor Berry and Doctor Thompson for this contribution. As was stated in their paper, Doctor Pool pointed out, in World War I, proper debridement of joints was essential if infection was to be prevented and this was made of record in the medical history of that war; yet during the peace that followed the war and when World War II came, the medical profession had not taken advantage of this information or had failed to read the literature which contained the answer. I hope that when we plan for the next war, or when it is imminent, someone will find and read this paper which has been presented here today.

Unfortunately, proper debridement was more often done in injuries to knee joints and other small joints than it was when the hip joint was involved. The proper debridement of a hip joint is a formidable operation and not too many surgeons are sufficiently trained to properly perform it. The hip joint lies deep in muscle structure and when involved in battle wounds is often complicated with visceral or multiple injuries or both.

If infection is to be prevented in joints, early proper debridement is essential. If this infection is not prevented the joint is destroyed and too often, in order to save a patient's life, a joint resection or an amputation is required. It is believed that the proper debridement of joints and compound injuries in civil life is as essential as it is in the Army.

DR. CARL EGGERS, New York: I arise to call attention to another phase of the subject, that is, that this presentation illustrates the importance of basic training of surgeons. Doctor Berry is at present known principally for his work in thoracic surgery. When he was confronted with war surgery his mind reverted to his early training and experiences. This emphasizes the great importance of not encouraging too early specialization, but to give all surgeons training in general surgery before they embark on a specialty.

DR. LEO ELOESSER, San Francisco: I would like to ask Doctors Berry and Thompson whether they closed the skin and soft parts, or left them open.

DR. EDWARD D. CHURCHILL, Boston: The points raised by General Kirk and Doctor Eggers are very important. Military surgery is a discontinuous specialty and stops when the last shot is fired, then is forgotten. We knew too little of the surgical experience of World War I. I was a member of the N. R. C. Committee assigned to prepare a manual of war surgery. If the men assigned these tasks had gone back to the literature of

World War I and based their manuals on the writings of the surgeons who participated in that conflict, the results would have been more helpful.

The second question brought up by Doctor Eggers—why did we have trouble getting these basic principles adopted by surgeons? Early in World War II we were dealing with specialists in civilian surgery, not with military surgeons. I personally pleaded with orthopedic surgeons to follow Doctor Berry's recommendation regarding the knee joint, but they thought it unsound to think of opening a knee joint in the operating tent of an Evacuation Hospital, quite forgetting that the dirt, torn uniform and devitalized cartilage within the joint was a far greater hazard than the tarpaulin flooring and other relatively crude provisions for aseptic surgery. It was impossible to convince the general surgeon that he should do a wide arthrotomy on a hip joint. He had never seen the operation and did not know the anatomy.

Dr. James E. Thompson, New York (closing): I wish to thank all the discussors. In reply to Doctor Trimble's question about causalgia, I think it is an interesting possibility as a cause of the pain. We have had no experience in treating such cases with sympathectomy. In the one case on which we were able to obtain a check-up x-ray examination there is a lot of arthritic reaction about the hip joint, which must be the cause of his pain. I would not be surprised if his hip joint has to be fused at a later date.

In answer to Doctor Eloesser, the skin was always left open, to be closed secondarily in a four- to seven-day period. We either closed them ourselves, or the closure was performed later at a general hospital.

PULMONARY CAVERNOUS HEMANGIOMA WITH ARTERIO-VENOUS FISTULA, SURGICAL MANAGEMENT: CASE REPORT*

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Visceral hemangiomas are uncommon. Autopsy records indicate an incidence less than 0.3 per cent. Hemangiomas of the lung are rare and for this reason I felt that my case should be added to the small group previously reported.

Hepburn and Dauphinee searched the literature to the time that they reported their case in 1942 and summarized their findings as follows, "Cavernous hemangioma of the lung is not mentioned in Henke and Lubarsch's Handbook of Pathology. This work, however, does refer to a case described by de Lange and de Vries-Robles (1923) of an infant age two and a half months, whose lungs, at autopsy, were seen to contain two small tumors, which microscopically were shown to be capillary hemangiomas. Wollstein in 1931 reported a malignant hemangioma of the lung which was found at autopsy in a child aged four months, and Hall in 1935, also described, a malignant pulmonary hemangioma in a woman aged 40. In both these malignant cases there was a distinct anemia and an appreciable lowering of the red blood count. Bowers, in 1936, reported the death of a new-born child caused by hemorrhage from a ruptured pulmonary angioma. In 1939, Duvoir et al. related the case of a child who, from 1932, had been subject to paroxysms of dyspnoea and who had congenital lues. Roentgen rays of the chest showed an opacity which was thought to be caused by a lipoma. Pathologic examination of the removed tumor, however, showed the mass in the lung to be a hemangioma. The child died of pneumonia five years later and autopsy revealed many lipomata, visceral angiomata and a lipoangioma. Cyanosis and clubbing of the fingers were not mentioned and no blood examination was recorded."

The review of Hepburn and Dauphinee included two additional cases, one reported by Rodes in 1938 and one by Smith and Horton in 1939. To these they added their case.

Rodes, it would seem, should be credited with the first description of pulmonary cavernous hemangioma as a clinical entity. In the eight years following his report ten additional cases have been recorded, including my case. Two deductions are evident; cases existing prior to 1938 were not recognized and second the lesion is not as rare as the above figure suggests.

Smith and Horton, accredited with having made the first ante mortem diagnosis, pointed out a characteristic clinical syndrome and its physiologic basis. And from the additional contributions from the case studies of Hepburn and Dauphinee, Goldman, Janes, Jones and Thompson, Adams, Thornton and

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Eichelberger, Shenstone and Makler and Zion a comprehensive picture of the entity and its pathologic and clinical variations has evolved.

The hemangiomas in most instances have been unilateral and near the hilus but in the cases reported by Rodes and Makler and Zion and in one of Janes' cases there were multiple hemangiomas involving both lungs.

How these lesions should be classified is of academic interest principally. Anatomically, they are hemangiomas, physiologically antero-venous fistulas. As a matter of fact, Reid, Horton and others are of the opinion that all hemangiomas are abnormal arteriovenous communications through which arterial blood flows from arteries to veins without passing through a capillary bed.

Probably all pulmonary hemangiomas are congenital. Their presence has been demonstrated in newborn infants and in some of the reported cases there has been a history of cyanosis since infancy. Why symptoms do not appear until later in life in some cases may be explained by the fact that cyanosis and symptoms associated with it result from a large shunt of blood from the pulmonary artery to the pulmonary veins. It has been estimated that at least 25 per cent of the blood must be shunted before cyanosis is apparent. It would seem reasonable to assume that a small fistula through a hemangioma would progressively enlarge to a size that would produce symptoms as time passed. There is no record of a pulmonary arterio-venous fistula of traumatic origin and, furthermore, in the reported cases there is no definite evidence of an etiologic factor other than a congenital one.

In terms of oxygen saturation the direction of blood flow through a fistula in the lung is the reverse of that through a shunt in the systemic circulation. Therefore, much of the blood leaving the left ventricle is venous and unsaturated with oxygen so that some degree of cyanosis is a constant symptom. The cyanosis is somewhat distinctive in that there is no associated enlargement of the heart or other evidence of a cardiac lesion but there is, with exceptions, a compensatory polycythemia, polyemia and hyperhemoglobinemia with an increased hematocrit and reduced oxygen saturation. The degree of cyanosis and polycythemia is dependent upon the size of the fistula and the volume of the shunt and the increase in the number of red cells accounts for the increased blood volume; there being no appreciable increase in serum and none in the number of white blood cells and platelets. The blood picture differs also from that of true polycythemia by absence of changes, such as basophilic stippling and immaturity of the white cells. A constant finding is the presence of one or more chronic non-progressive pulmonary lesions which roentgenographically are cylindrical masses and which under the fluoroscope often may be observed to pulsate. In laminagrams the cylindrical configuration and branching character of the lesions may be demonstrated.

In five of the reported cases and in my case a continuous murmur was heard over the pulmonary lesion and in each instance it was loudest at the end of deep inspiration.

Clubbing of the fingers and toes is a constant finding. The extent of these changes varies with the duration and the degree of cyanosis.

Other symptoms are variable including pain in the chest, cough, dyspnoea, asthmatic paroxysms, hemoptysis, fatigue, vertigo, faintness, headaches, syncope and disturbances of speech and vision.

Treatment consists of ablation of the fistula. This can be accomplished only by surgical interference. Operation is indicated in the absence of incapacity and even in the absence of noteworthy symptoms because of risk of fatal hemorrhage from rupture of the hemangioma and of sequelae resulting from thromboses secondary to the polycythemia.

Seven cases including mine have been operated upon and all have been cured. In four, (Shenstone and Janes, one; Jones et al., one; Adams et al., one and Goldman's case) a total pneumonectomy was done, in two, including my case a lobectomy and in one, a case of Janes, local excision of multiple bilateral lesions. The ideal operation would eradicate the hemangioma by interrupting the vessels communicating with it without sacrificing pulmonary tissue. Unfortunately, this has been technically impossible except in Janes' case.

REPORTED CASES

In 1938 Rodes reported a 25-year-old male with a history of cyanosis and dyspnoea as long as he could remember and clubbing of the fingers since the age of 15. His heart was normal and there was no congenital defect. He died of a massive hemorrhage from a ruptured hemangioma. His red blood cell count was 7,540,000 and the hemoglobin 118 per cent. A roentgenogram showed spherical shadows in both lower lung fields. Postmortem examination revealed hemangiomas both lower lobes, two in the right and one in the left.

The second case and the first one diagnosed ante mortem was reported in 1939 by Horton and Smith. Their patient, a male of 47 years, stated that he had been a "blue" baby at birth and had been aware of cyanosis and of clubbing of the toes and fingers since the age of 24. When first examined by Horton and Smith in 1932, there was in addition to the cyanosis and clubbing a polycythemia, a red cell count of 6,000,000 and a hemoglobin of 20.6 Gm. leading to a diagnosis of polycythemia vera. When re-examined six years later a continuous murmur was heard at the base of the right lung. A roentgenogram of the chest showed a shadow of increased density in the right posterolateral lung field. This was demonstrated to be a vascular tumor by injection of radiopaque solution into the basilic vein.

Hepburn and Dauphinee in 1942 reported the third case and the first one cured by operation. This patient, a female of 23, complained of dyspnoea, attacks of dizziness, faintness and thickness of speech, cyanosis and clubbing of fingers and toes. The red blood cell count was 9,600,000, hemoglobin 140 per cent, and total blood volume 8,500 cc. Oxygen saturation of the arterial blood was 70 per cent. An X-ray film of the chest revealed a shadow in the right middle and lower lobes. No bruit was heard over this area. A right total pneumonectomy was done by Shenstone and Janes and a cavernous angioma was demonstrated in the resected lung. There was a rapid and complete relief of symptoms and signs.

Goldman in 1943 reported a man of 22 who had had slight cyanosis since infancy. For seven years there had been increasing cyanosis, dyspnoea and frontal headaches and at the time of admission the additional complaints of weakness, nausea and vomiting. The red blood count was 11,450,000, the hemoglobin 137 per cent, oxygen saturation of the arterial blood 70 per cent, blood volume 8,170 cc. and plasma volume 2,450 cc. A dense shadow in the left lung field was demonstrated by means of laminagrams and a kymiogram to be a solid branching mass with an intrinsic pulsation which was synchronous with that of the pulmonary artery.

Treatment with roentgen rays, radioactive phosphorous and venesection was ineffective. A total pneumonectomy resulted in complete relief of symptoms.

Recently Goldman reported that his patient has a brother, 32 years of age with the same but less severe clinical picture.

Janes in 1944 reported a man, 30 years of age who had coughed up bright blood on several occasions over a period of two years. His lips and fingernails were definitely cyanotic and there were multiple small hemangiomas on the lower lip. A soft blowing murmur was heard in the region of the right cardiophrenic angle. Radiographs of the chest showed two shadows in the right lung and one, or possibly two, in the left. There was no polycythemia.

The hemangiomas in both lungs were subpleural and were locally excised. The right side was operated upon first and two separate lesions removed, one by individual ligation of the vessels entering the hemangioma and the other by resection between clamps. Six months later the two lesions in the left lower lobe were excised. He recovered without incident.

In discussion of a paper by Jones and Thompson (abstracted below), Janes mentioned another case upon whom Shenstone and Janes performed a lobectomy for a hemangioma with cyanosis but no polycythemia.

In 1944 Adams et al. reported a man 24 years old complaining of frequent nosebleeds and colds for three years and of a cyanosis and of clubbing of the fingers and toes for at least 16 years. Examination revealed extreme cyanosis, marked clubbing of fingers and toes and several small hemangiomas of the lip and face. The red blood count was 7,200,000 the hemoglobin 23.0 Gm., the hematocrit 82 per cent, the vital capacity 3,800 cc., the total blood volume 12,750 cc., the plasma volume 2,420 cc. and the oxygen saturation of the arterial blood 71 per cent. Roentgenograms of the chest showed a lobuated moderately opaque area measuring 25 sq. cms. between the 7th and 9th rib posteriorly in the left lung and a second similar but smaller opacity in the right lung.

A left total pneumonectomy was done. Convalescence was uneventful and there was rapid restoration of normal blood volume, red blood cell count and oxygen saturation of the arterial blood and disappearance of cyanosis and other symptoms.

Jones in 1944 reported a woman aged 24 years. She had been very cyanotic since birth and had had increasing clubbing of the fingers since nine years of

age. Examination revealed in addition to the cyanosis and the clubbing of finger and toes, a loud, rough roaring murmur probably continuous and loudest at the end of inspiration over and just beneath the right breast.

Roentgen studies including planigrams showed an 8 or 10 cm. rounded area of increased density in the right lower lung field with communicating masses interpreted as dilated branches of the pulmonary artery. Fluoroscopically the whole thing seemed to pulsate. The mass at one area appeared calcified. The red cell count was 7,080,000, hemoglobin 130 per cent, plasma volume normal and whole blood volume 170 per cent.

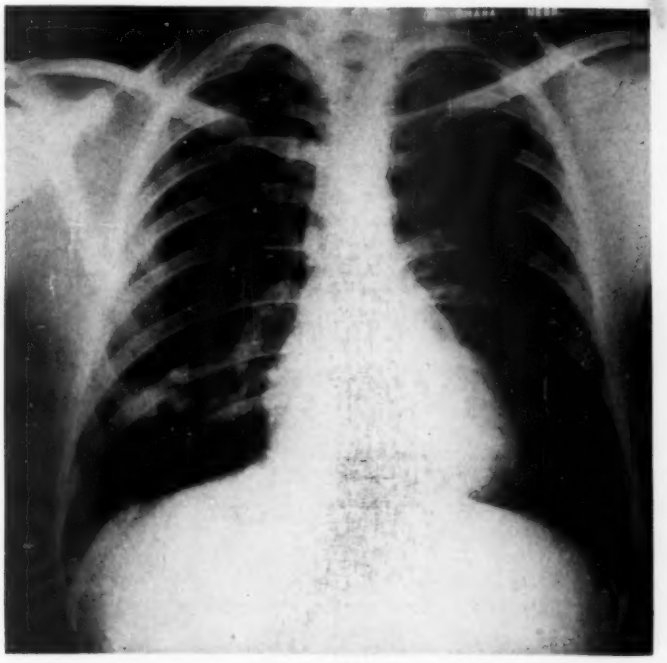

FIG. 1.—3 x 4 cms. ovoid shadow of increased density in the lower right lung field at the level of the 9th rib and 11 cms. from the midline. In lateral view it was posterior. Note two tortuous linear shadows extending from the mass toward the hilus. These are no doubt dilated pulmonary vessels.

A right total pneumonectomy was followed by immediate disappearance of cyanosis and a prompt return of the blood to normal and a cure.

In 1946 Makler and Zion reported a man 20 years of age with a history of marked cyanosis, slight dyspnoea and occasional headaches and nosebleeds for three years. Examination revealed telangiectasis behind the right ear, cyanosis and clubbing of the fingers and toes. The red cell count was 7,700,000 and the hemoglobin 19.5 Gm. Roentgenograms showed four rounded shadows, three in the right lower and mid-lung fields and one in the left mid-lung field. The

Valsalva experiment was positive and laminagrams showed a worm-like configuration of the masses and a continuation of these masses with linear shadows from the hilus.

The patient had insufficient incapacity to desire and warrant operation.

CASE REPORT

A railroad switchman of 29 was admitted to the Union Pacific Department of Saint Joseph's Hospital, July 17, 1946. He had pneumonia eight years ago and since then progressive dyspnoea on exertion, nocturnal asthmatic attacks and a dry cough. He had

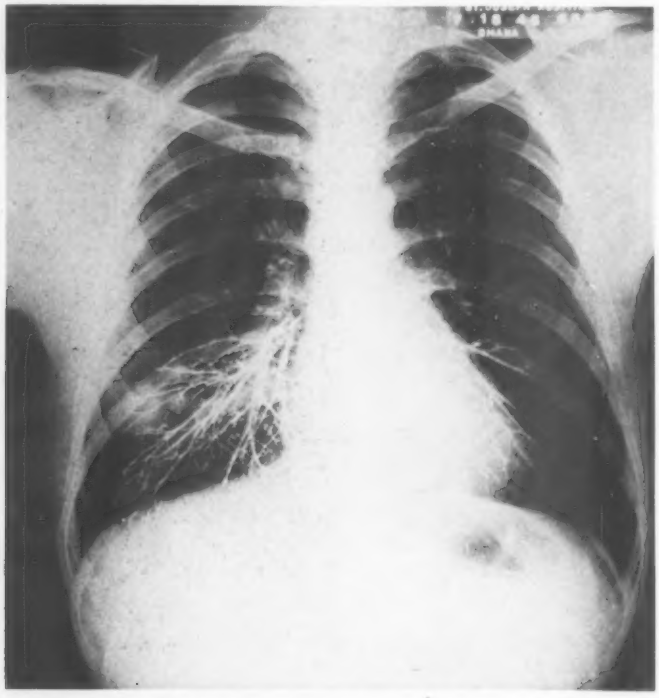

FIG. 2.—This bronchogram places the shadow in the lower lobe and indicates that there is no association to the bronchial tree.

been aware of cyanosis of his lips and fingernails for six years. During the last three years he had several attacks of loss of consciousness which lasted only a few minutes, frequent headaches and episodes of blurring of vision, and chronic fatigue. For one year there had been a dull pain along the right sternal border and for three months he had been unable to work on account of fatigue and breathlessness on exertion.

The positive findings in the physical examination were: Moderate cyanosis, slight clubbing of fingers and toes, multiple small blue hemangiomas of lips, dyspnoea from climbing half a flight of steps, a vital capacity of 2,800 cc., a rough continuous murmur over the lesion under the right eighth rib in the posterior axillary line, louder on inspiration and a blood pressure of 95/65 in both arms. Blood studies revealed a hemoglobin of 18 grams, red blood cells, 6,800,000, white blood cells 8,300 with a normal differential and a hematocrit of 71 per cent. Blood volume and its oxygen volume and tension were not determined. The electrocardiogram was normal.

The roentgenologic report was as follows: There is a sharply delineated ovoid nodular shadow of increased density measuring 3 x 4 cms., lying well posterior and 11 cms. to the right of the midline at the level of the 9th rib in the posterior axillary line. Bronchograms of both lower lung fields show no evidence of bronchiectatic change and no communication between the nodular lesion and the bronchial tree. (See Figs. I and II.) A diagnosis of arteriovenous fistula of the right lower lobe was made. Under intratracheal cyclopropane anesthesia and through the 7th intercostal space the right pleural cavity was opened. There were no pleural adhesions and the interlobar fissure was well defined but there was no middle lobe. Throughout the entire lower lobe there was a thrill which disappeared upon digital compression of the vessels to the lower lobe near the hilus and over the lobe at the point of maximum intensity of the thrill. The lower lobe was removed by dissection and individual ligation technic. The upper lobe was expanded and expansion maintained with constant suction through two air-tight catheters. Chemotherapy started 24 hours preoperatively was continued for five days. Blood was not given. Oxygen was administered for 24 hours. The patient made an uneventful convalescence and has remained free of symptoms. Examination, two and one half months after operation, revealed no cyanosis, a hemoglobin of 13.5 Gm., a red blood count of 4,200,000, white blood cells 6,800 with normal differential and a hematocrit of 53 per cent. The vital capacity was 3,200 cc.

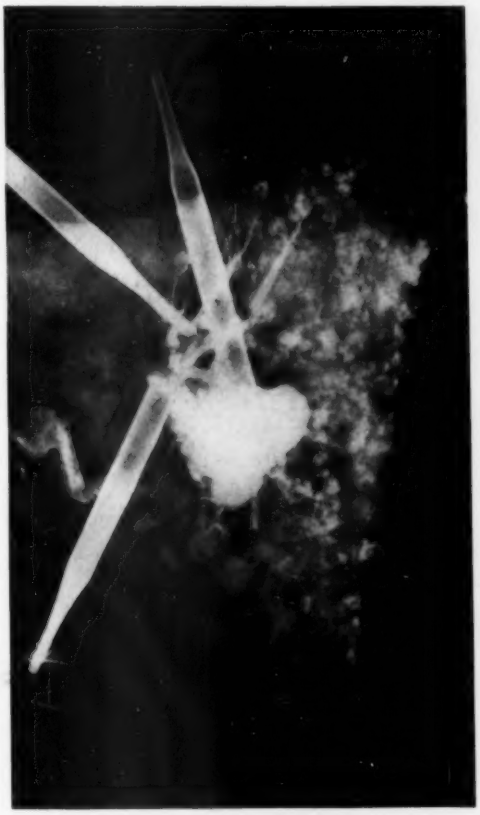

FIG. 3.—Roentgenogram of the excised right lower lobe after injection of a thin aqueous barium suspension into the pulmonary artery through the left upper cannula. The other two are in pulmonary veins and are filled with the suspension as is the distended hemangioma, demonstrating the shunt. The incomplete filling of ramification of the pulmonary artery indicates that passage through the fistula is the way of least resistance and the course which was followed by most of the blood passing through that lobe.

The resected lobe was injected with a barium mixture through a cannula in the pulmonary artery. The mixture returned freely through the pulmonary veins. A roentgenogram of the injected specimen appears in Figure III.

Dissection of the lobe revealed two cavernous hemangiomas measuring 2 x 4 cms. and 1 x 2 cms. Vessels communicating with these spaces were not demonstrated.

CONCLUSIONS

1. Cavernous hemangioma of the lung is a relatively rare lesion but not as rare as the number of reported cases suggests.

2. It is probably a congenital lesion and may exist without symptoms until an arteriovenous shunt becomes established or of such a size as to cause con-

siderable reduction in the oxygen saturation of the arterial blood. There is then a characteristic syndrome; a demonstrable pulmonary lesion which may be demonstrated to have characteristics of a vascular tumor by roentgenographic studies and an associated generalized cyanosis with clubbing of the fingers and toes. In most cases, but not invariably so, there is a compensatory polycythemia.

3. Treatment consists of ablation of the vascular fistula. Ideally this should be accomplished without sacrificing pulmonary tissue as has been done in one case. Usually this is technically impossible and eradication can be accomplished only by means of a lobectomy or pneumonectomy. Since there is much hazard of a fatal hemorrhage or of thrombotic sequelae from an associated polycythemia, surgical interference is indicated in the absence of incapacity and even in the absence of troublesome symptoms if there are no additional factors to increase seriously the risk.

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CONTROL OF HEMORRHAGE FROM WOUNDS OF THE HEART BY THE GELATIN SPONGE "PATCH" TECHNIC*†

A New Experimental Method

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IN SEVERAL PREVIOUS COMMUNICATIONS, the absorption[1] and hemostatic action of gelatin sponge have been presented. In a series of 30 experiments on dogs, the bleeding from wounds of the liver, kidneys, and spleen was controlled by the gelatin sponge.[2] In another series of 12 experiments, a lobe of the liver was resected and the hemorrhage controlled by a "blanket" of gelatin sponge applied over the resected stump.[3] In 36 experiments on dogs, wounds were made in veins of which 28 were in the vena cava.[3] The bleeding was stopped by a "patch" of gelatin sponge except in two experiments where the animals died of uncontrolled hemorrhage at the time of operation and in one experiment where there was secondary hemorrhage. In a series of 17 experiments where wounds were made in the aorta of dogs, the bleeding was controlled by a cuff of gelatin sponge wrapped about the vessel and supported by a sheath of chromic catgut.[4] These experiments were performed for the most part without the addition of thrombin to the gelatin sponge and without any supplementary suturing. In view of the satisfactory results which were generally obtained in these experiments, the possibility of using the gelatin sponge by the "patch" technique for wounds of the heart naturally suggested itself. A preliminary report of this technique has been made.[5]

EXPERIMENT

The dogs were anesthetized with ether and an intra-tracheal tube inserted. The anesthesia was maintained during the operation with positive pressure. Under ordinary aseptic technic the chest was entered through the fifth intercostal space and the heart exposed. The lungs were retracted and the pericardial sac was opened. A stay suture was passed through the apex of the heart for traction. A wound was then made in the right or left ventricle with a scalpel (Fig. 1) and often enlarged with scissors (Fig. 2) to permit a rather

* Read by title before the Meeting of the American Surgical Association, March 25–27, 1947, Hot Springs, Virginia.

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profuse spurt of blood with each systole (Fig. 3). In some instances the wound was made large enough to admit the tip of the finger. A sheet of dry, compressed gelatin sponge,* which had been cut to approximately one and one-half inches in diameter, was applied over the spurting wound and held in place by the operator's fingers with moderate pressure synchronized with the contractions of the heart while traction was made on the suture passed through the apex (Fig. 4). Pressure was maintained over the patch for three to five minutes for wounds of the right ventricle and five to 13 minutes for wounds of the left ventricle. After this period of time the "patch" was usually sufficiently

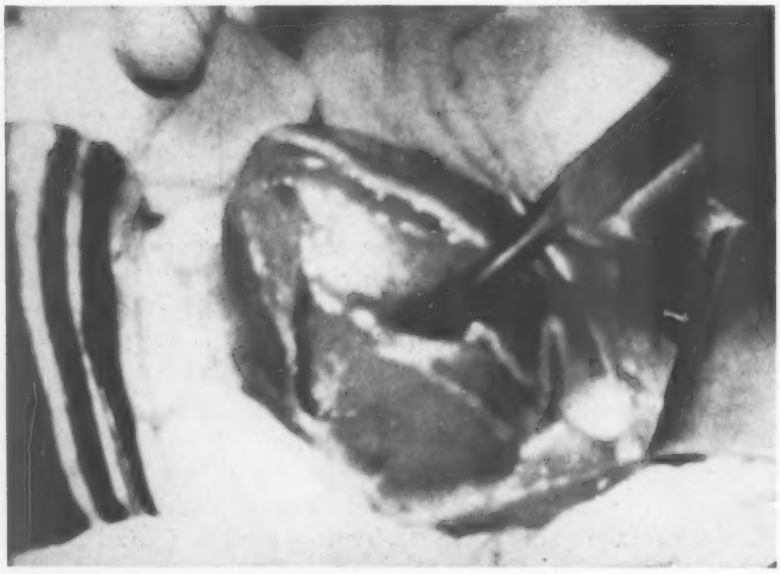

FIG. 1.—Showing scalpel wound of left ventricle.

adherent to control the hemorrhage completely. After 20 to 30 minutes the "patch" was usually firmly adherent to the heart and sometimes difficult to remove because of its "fibrin fixation" to the wound (Fig. 7). The pericardium was sutured and the wound in the chest closed with silk after re-expanding the lungs with the intratracheal positive pressure and withdrawing any residual air in the pleural cavity by a catheter which was withdrawn as the last suture was placed in the wound.

During the period of pressure on the patch, the sponge was permitted to become saturated with blood (Fig. 5). It was a rather important point in the

* The gelatin sponge used in these experiments had been heat sterilized and packaged in large sealed glass jars by the manufacturer. The sponge was provided in the form of sheets measuring 3¼ inches by 4¾ inches by ½ inch. When compressed the sponge measured about ⅛ inch in thickness. The smaller pieces of sponge which had been commercially available were found to be entirely inadequate in controlling massive hemorrhage such as was produced in these experiments.

FIG. 2.—Showing wound of ventricle being enlarged with scissors.

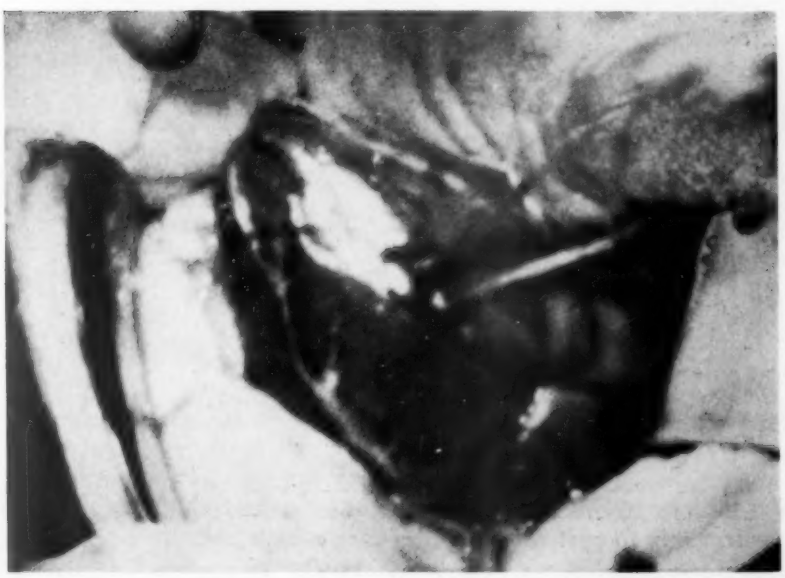

FIG. 3.—Showing hemorrhage from wound of left ventricle.

technic to maintain even pressure on the patch so that when the blood clotted in the sponge, the "patch" would become adherent about the wound as a result of the liberation of fibrin during the clotting process (Fig. 6). If the blood

FIG. 4.—Showing "patch" of dry compressed gelatin sponge applied over spurting wound of left ventricle.

FIG. 5.—Showing "patch" of gelatin sponge being held in place over wound of left ventricle after it has become saturated with blood.

clotted in the sponge before even pressure was obtained, the "patch" would not adhere sufficiently to control the hemorrhage completely. In several instances it was necessary to reinforce the original "patch" or apply a fresh one on the wound. This latter was found to be more satisfactory.

Another point in technic was to avoid having the "patch" become adherent to the gloved fingers while pressure was being maintained. The dry compressed sponge would stick to the gloved fingers very easily. Moistening the gloves with saline solution just before applying the "patch" would usually suffice to prevent this. In subsequent experiments on the use of the "patch" for wounds of the auricles an improvement in the technic of applying the "patch" was worked out.[6] This consisted of using a piece of perforated Cilkloid over the "patch" to prevent the sponge from sticking to the gloves. The Cilkloid would become adherent to the "patch" if there was any remaining sponge which was not soaked by blood. By applying a few drops of saline over the Cilkloid, it would penetrate the perforations and moisten and soften the sponge

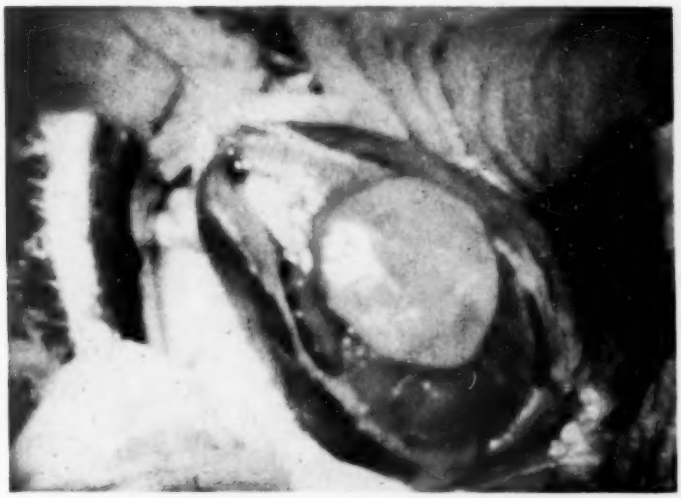

FIG. 6.—Showing "patch" of gelatin sponge which has become adherent to heart due to the clotting of blood in the sponge and completely controlling hemorrhage from wound in heart (left ventricle).

so that the Cilkloid could be easily removed without danger of dislodging the gelatin sponge patch. Needless to say the Cilkloid should always be removed as there is no evidence that it would become absorbed, and furthermore it is possible that its behavior in the tissues would resemble that of cellophane.

RESULTS

In a series of 15 experiments, the wound was made in the right ventricle in 4 and in the left ventricle in 11. The hemorrhage was completely controlled by the application of a gelatin sponge "patch" and the animal survived the immediate postoperative period. In six other experiments, the animal died from ventricular fibrillation when the pericardial sac was opened or when the wound was made in the heart. Novocaine solution and electrical stimulation were used in an attempt to prevent or arrest ventricular fibrillation. These

measures were, for the most part, relatively ineffective. The most satisfactory means of preventing fibrillation appeared to be careful handling of the heart and especially avoiding torsion. Most of the instances of ventricular fibrillation occurred in the earlier experiments. In addition to these procedures, three acute experiments were performed without asepsis to work out points in the technic of applying the sponge. In these experiments the "patch" was applied, removed, and fresh "patches" reapplied as many as six times, with complete control of hemorrhage in each instance. These animals were sacrificed at the end of the experiment.

FIG. 7.—Showing gelatin sponge firmly adherent to heart 30 minutes after application of "patch." It is difficult to remove patch after this length of time due to the "fibrin fixation" of the sponge to the heart wound.

In the series of 15 animals which survived the wound of the heart to which the gelatin sponge "patch" was applied, five died between two and 12 days from distemper, pneumonia, or empyema. One died after three days from pneumonia but also had an intracardiac thrombosis due to the migration of the sponge "patch" into the cardiac chamber. In this particular experiment, the sponge was applied over a very large wound and it was necessary to place a second "patch" over this. It was the under "patch" which worked itself into the wound and contributed to the intra-cardiac thrombosis. Eight of the animals were sacrificed on the 4th, 18th, 24th, 40th, 68th, 73d, 92nd, and 104th day, and one was sacrificed after 6 months.

The heart specimens were photographed (Fig. 8), the cardiac chambers were opened, and sections were taken through the wound in the myocardium for microscopic studies. In two of the animals, there was a greyish appearance

FIG. 8.—Showing gross specimen of heart at autopsy at varying periods of time after application of gelatin sponge "patch" for control of hemorrhage from wound of heart.

A. After four days.

FIG. 8B.—After nine days.

to the pericardial sac suggestive of an early pericarditis although no exudate was present. This was usually associated with an extensive distemper, pneumonia, or empyema.

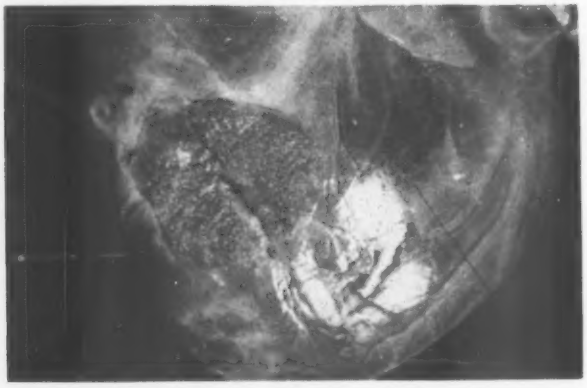

FIG. 8C.—After 18 days.

FIG. 8D.—After 40 days. The sponge has undergone partial absorption.

In none of these experiments was there any evidence of accumulation of blood in the pericardial sac to suggest that secondary hemorrhage had occurred from dislodgement of the "patch." The closure of the pericardium appeared to be adequate additional support to the sponge to prevent subsequent blowing off

of the "patch." There was no evidence of aneurysm formation in the ventricular wall where the wound was produced in any of the specimens examined.

At autopsy the gelatin sponge "patch" was very firmly adherent to the heart, and usually only lightly adherent to the overlying pericardium. There was very little evidence of adhesions within the pericardial cavity except where the sponge was present. As the sponge underwent absorption, the adhesions present tended to regress.

From the gross standpoint, the sponge appeared to undergo absorption in about two months. In the microscopic studies, an early stage of sealing off of

FIG. 8E.—After 68 days. The gelatin sponge has undergone absorption and there is a residual fibrous tissue scar overlying wound which was adherent to pericardium.

the wound by the gelatin sponge "patch" and filling of the wound by a blood clot was seen. Relatively rapid fibroplasia was found to develop, uniting the wound and the intact muscle under the cover of the gelatin sponge. After several weeks the wound was healed by a well differentiated fibrous tissue scar (Fig. 9).

In two instances there was calcification in the healed scar of the myocardium. The gelatin sponge apparently produced relatively little inflammatory reaction and it was unusual to see much of a polymorphonuclear invasion in the

early stages except in those animals where there was a complicating infection. There was replacement of the sponge by fibrous tissue due to the invasion of the sponge by fibroblasts during the period of healing of the wound.

The rate of absorption of the sponge as determined by microscopic studies was found to be somewhat slower than was observed in previous work. In one instance there was evidence of a few remnants of the sponge in a thin fibrous scar as late as three months, although the sponge was usually completely absorbed in about two months.

FIG. 9A.—Showing photomicrograph of heart after nine days. The gelatin sponge "patch" covers wound in which extensive fibroplasia has filled in the defect in the myocardium. In addition there are areas of calcification in the healing wound.

COMMENT

The control of hemorrhage from a wound of the left ventricle by the use of dry, compressed gelatin sponge without the addition of thrombin or supplementary suturing represents a critical experimental test of the effectiveness of this hemostatic agent. Furthermore, this study has given additional information on the mode of action of the gelatin sponge.

It would appear that the sheet of dry, compressed gelatin sponge acts more or less like a tampon which stops the stream of blood coming out of the wound. When the sponge is soaked in saline it is so soft and so easily permeated by blood that it does not lend itself to controlling a forceful stream of blood such

FIG. 9B.—Showing photomicrograph of healed wound in left ventricle with remnants of gelatin sponge overlying the fibrous scar which can be traced through the wall of the ventricle after 40 days.

as one encounters from the left ventricle. As the dry sponge is held over the wound enough blood escapes through the intercommunicating interstices to saturate the sponge. When the blood clots in the sponge one has obtained essentially a reinforced clot with the sponge architecture offering a framework for the clot. As the blood clots in the sponge, fibrin is liberated and produces

an increasingly strong adherence of this reinforced clot or "sponge clot" to the wound provided that even pressure is applied over the sponge during the clotting process. It is necessary to maintain this pressure until the adherence of the "sponge clot" to the wound is sufficiently strong that it will withstand the force of the blood from the cardiac chamber. This was found to require as long as 13 minutes in some of the experiments on the left ventricle although only three minutes was required in some wounds of the right ventricle.

FIG. 9C.—Showing photomicrograph of heart 68 days after application of gelatin sponge "patch" to wound. There is a residual fibrous plaque replacing the gelatin sponge and covering the fibrous scar in the myocardium.

In view of the fact that thrombin was not used with the gelatin sponge in these experiments it would suggest that the clotting was brought about by a combination of factors. The stopping of the stream of blood from the heart wound by the tampon effect of the dry sponge is one important factor. In several instances where relatively small wounds were made, especially in the right ventricle it was possible to remove the gelatin sponge "patch" after about 10

minutes without having a resumption of the hemorrhage from the wound due to the formation of a clot which sealed the wound edges together. On the other hand the removal of a "patch" would usually result in the resumption of hemorrhage in most instances. One of the principle sources of thromboplastin is heart muscle and it is probable that in wounds of the heart there may be an appreciable amount of clot stimulating material liberated which enters the sponge along with the blood and thus hastens the formation of a clot in the sponge as well as in the wound. Furthermore, the enormous surface area of

FIG. 9D.—Same as 9C showing fibrous scar in myocardium.

the many interstices of the sponge would undoubtedly cause damage to the platelets, thus liberating thromboplastin from this source. The thromboplastin along with the calcium and prothrombin of the blood probably produced enough thrombin to initiate the clotting mechanism by its action on the fibrinogin.

Aside from the hemostatic effect of the sponge, it should also be pointed out that the sponge "patch" provided protective cover to the wound and gave it support during the process of wound repair. This was also observed in previous studies. After completing its primary role as a hemostatic agent and its secondary role of protection and support of the wound during the healing

process, the gelatin sponge underwent absorption with nominal tissue reaction.

It is very important to emphasize that the successful use of the gelatin sponge revolves about attention to the details in the technic of applying the sponge. This may come only from actual experience in handling this material.

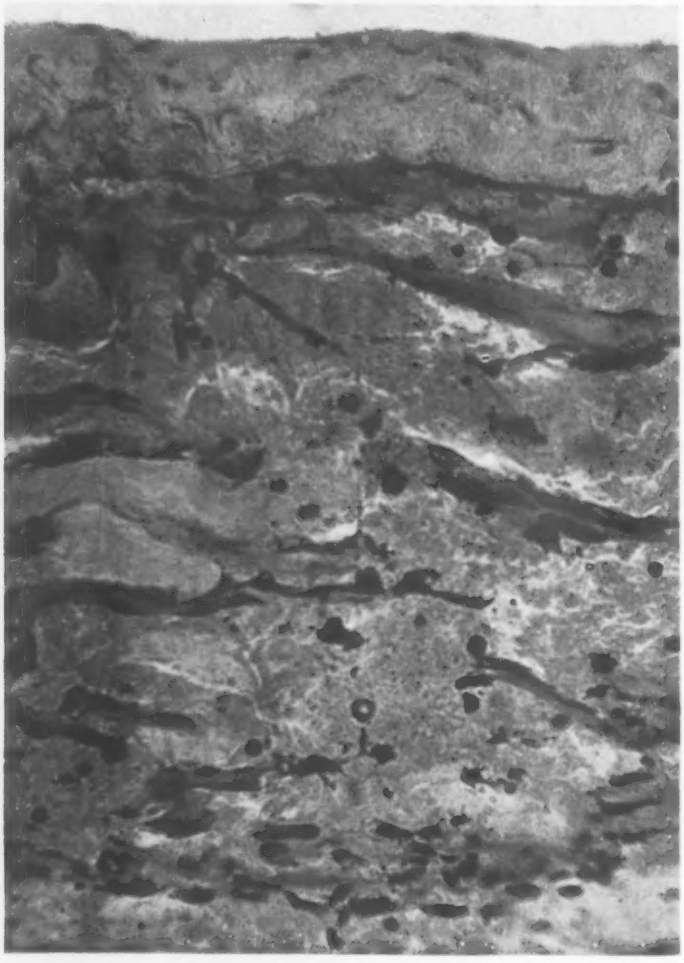

FIG. 9E.—Same as 9C showing higher magnification of fibrous plaque overlying wound in which a few spicules of gelatin sponge can still be detected. These remnants are undergoing the terminal phase of absorption by the action of the adjacent macrophages.

In addition, an understanding of the mode of action of the sponge in obtaining hemostasis aids in working out the technique which may be applicable to any particular problem of hemostasis.[7]

In view of the results obtained in this experimental study, it would suggest that the gelatin sponge may have a place in the surgical treatment of penetrating wounds of the heart.

Since the first successful suture of a wound of the heart by Rehn in 1896[8]

there have been many advances in surgery of the heart. The principal contributions to the treatment of wounds of the heart have been made by Elkin,[9] Bigger,[10] Beck,[11] Singleton,[12] Griswold and Maguire,[13] and Linder and Hodo.[14] With improvement in operative technic and asepsis, and with attention to administration of intravenous fluids preoperatively as advocated by Cooper and co-workers[15] it has been possible to obtain increasingly satisfactory results from suture of wounds of the heart. This is demonstrated by the most recent series of cases reported by Elkin where a mortality rate of 22 per cent was obtained.

Blalock and Ravitch[16] have drawn attention to the desirability of conservative management of selected cases of wounds of the heart by resorting to aspiration of the pericardial sac to relieve the cardiac tamponade. In the presence of continued bleeding into the pleural cavity or through the chest wound or if evidence of cardiac tamponade recurs after aspirations they feel that immediate cardiorrhaphy should of course be performed.

Although we have presented a non-suture experimental method of dealing with wounds of the heart, in the clinical application of this experimental study we are not prepared to suggest that the gelatin sponge should be used to replace suture.

One of the main problems in the handling of stab or bullet wounds of the heart in patients is the massive hemorrhage which one may encounter as one opens the pericardial sac. The gelatin sponge may provide a means of obtaining immediate control of hemorrhage from a wound of the heart and at least momentarily preventing further loss of blood. It is thoroughly possible that with the hemorrhage controlled in this fashion, one could then very gently peel back the sponge and insert sutures in a relatively dry field. Or the sutures may be placed in the wound and tied over the patch of sponge covering the wound.

Another point which suggests itself is that the gelatin sponge may provide a secondary line of defense after sutures have been placed in the wound and thus serve as an additional safeguard against leakage from the suture line. This may make it possible to place fewer sutures and to tie them with less tension, thus lessening the danger of ischemia of the cardiac muscle or of initiating a stimulus which may precipitate ventricular fibrillation.

Finally, in relatively small wounds, or in wounds which are adjacent to coronary vessels, it is possible that the gelatin sponge "patch" alone may suffice. The clinical evaluations of this experimental method must be made by those who have had the widest experience in the treatment of penetrating wounds of the heart. It has come to our attention that the gelatin sponge has been used in two instances as a supplement to suture of a wound of the heart.[17] In one of these cases it was especially useful in controlling bleeding where the stay suture had been placed for traction.

Furthermore, it is hoped that some modification of this gelatin sponge patch method may be helpful in controlling hemorrhage in other types of cardiac surgery, such as for valvular stenosis or foreign bodies.

SUMMARY

In a series of 15 experiments on dogs, it has been possible to control hemorrhage from relatively large wounds of the right or left ventricle with a "patch" of gelatin sponge without any supplementary suture or the use of thrombin in the sponge.

The fundamental principles involved in the control of hemorrhage by the gelatin sponge "patch" is essentially as follows: When the dry compressed gelatin sponge is applied over the spurting wound it acts first of all as a tampon to slow down and stop the massive flow of blood through the wound. As the sponge becomes saturated with blood, clotting occurs in the sponge, thus forming a "reinforced clot." During the clotting process fibrin is liberated, which permits this reinforced clot or "sponge-clot" to adhere to the heart. In applying the "patch," it is therefore necessary to allow the sponge to become soaked with blood and then to maintain firm even pressure over the sponge until sufficient fibrin is liberated to produce the adhesive effect which is so essential to the control of the bleeding. Healing progresses under the protective cover of the sponge while the sponge gives support to the wound during this healing phase. The sponge ultimately undergoes absorption.

CONCLUSION

In view of these experimental observations, it would appear that the gelatin sponge may have a place in the treatment of wounds of the heart to control the immediate hemorrhage, as a supplement to suture, or possibly as an alternate to suture under special circumstances such as proximity of the wound to a coronary vessel.

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ANNOUNCEMENT

UROLOGY AWARD

THE AMERICAN UROLOGICAL ASSOCIATION offers an annual award of $1,000.00 (first prize of $500.00, second prize $300.00 and third prize $200.00) for essays on the result of some clinical or laboratory research in Urology. Competition shall be limited to urologists who have been in such specific practice for not more than five years and to residents in urology in recognized hospitals.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Hotel Statler, Boston, Massachusetts, May 17–20, 1948.

For full particulars write the Secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tennessee. Essays must be in his hands before March 1, 1948.

FAMILIAL HEMOLYTIC ANEMIA AND ITS SURGICAL ASPECT WITH SPECIAL REFERENCE TO A CASE COMPLICATED BY THE RH FACTOR*

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AND

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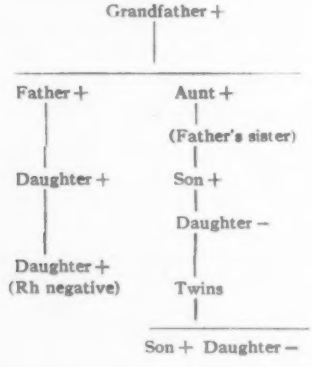
FROM THE PFEIFFER SURGICAL CLINIC OF THE ABINGTON MEMORIAL HOSPITAL

THE OCCURRENCE OF A CASE OF FAMILIAL HEMOLYTIC ANEMIA in the Pfeiffer Surgical Clinic of the Abington Memorial Hospital, which was complicated by the Rh factor and presented certain other interesting factors, prompted the authors to report the case and review the literature.

Familial hemolytic anemia, known for years as congenital hemolytic jaundice, may appear in the infantile form striking at birth, or be latent appearing anywhere from birth to the fifth decade, but less frequently after the third. It is believed to be a Mendelian dominant, but there is no regularity in its transmission nor severity.

TABLE I

THE PENHALLOW FAMILY



* +victims of disease.

It is interesting to note that the Rh factor is dominant and follows the Mendelian law of inheritance.[9] However, checking the Rh factor of this family showed that only one daughter was negative.

The acute exacerbations of this disease, we believe, are the result of some activation, possibly some antigen agglutinin or other allergic reaction. Once the activity begins it is apt to continue until the site of the increased hemolytic activity is removed.

* Read by title before the Meeting of the American Surgical Association, March 25, 26 and 27, 1947, Hot Springs, Virginia.

SYMPTOMATOLOGY

The symptoms of the disease are varied, but at no time appear to be very severe except during a crisis, and the patients are therefore rarely incapacitated; although they may be running a markedly elevated temperature, and be quite icteric, so much so that Chauffard remarked that the patients are "more jaundiced than sick." The jaundice varies in degree, but usually mild—being yellow or frequently sallow, rather than brown or green. Pruritus and bradycardia, so frequently a concomitant finding in jaundice, are not present.

The patients as a rule are subject to moderate weakness, malaise, and headaches. During a hemolytic crisis, which is an exacerbation of increased hemolytic activity, all the symptoms are increased, particularly the fever which may reach 105° or 106° without showing any marked effect on the patient's general well being; although in our experience gastro-intestinal symptoms, *i.e.*, nausea, abdominal pain, and diarrhea, are usually present.

The crises of hemolytic jaundice may be classified by various prominent features. Gripwall[6] classes them as (1) thermic; (2) abdominal; (3) essential blood crises. Thermic crises, apart from other aspects of the disease, are not clear. Abdominal crises apparently are associated with changes in liver function and structure, and not necessarily with increased blood destruction. The essential blood crises are what we commonly associate with acute crises of congenital hemolytic jaundice, and are of the hemoclastic type producing severe, even fatal anemia. The nature and relationships of the above three types cannot be definitely established as yet.

The spleen which is enlarged in nearly every active case and usually extends to the level of the umbilicus or below, may enlarge considerably during crises accompanied by more or less severe upper left quadrant pain due both to the stretching of the capsule and to occasional infarcts.

The liver may also be enlarged and during a crisis may likewise be quite tender. Liver crises according to Lewis[1] "may be precipitated by the passage of thickened bile through the ducts." Gastro-intestinal symptoms, as a whole, are common, but being referable particularly to the gallbladder. Hepatitis, cholecystitis, and cholelithiasis are common and give symptoms characteristic of these disorders.

Unexplained obdurate ulcers of the foot and ankle have been frequently observed. Osseous changes, such as thickened and enlarged parietal and frontal bones and mottling of the marrow spaces, also occur not infrequently (Türmschadel).

LABORATORY STUDIES

Blood studies are quite pathognomonic of the disease. The anemia which is microspherocytic in form may vary from three or four million to one million during a crisis. The color index and mean corpuscular hemoglobin are usually high. The mean corpuscular volume may be increased despite small mean corpuscular diameter. Anisocytosis is quite frequent and microspherocytosis is the conspicuous feature. Poikelocytosis may also be present. Reticulated red cells vary with the need of increased blood production and may vary from 2

to 60 per cent. Nucleated red cells are usually constant, showing evidence of cell regeneration. Usually the increased fragility of the red cells to the hemolytic action of hypotonic salt solution is characteristic, but it may be normal or even lessened if the reticulocyte count is elevated. The white cell response is not characteristic, but most frequently there is a leukocytosis with a polymorphonuclear increase. The platelets are usually normal.

The plasma volume is usually decreased; therefore the quite frequent dehydrated appearance of these patients.

The blood chemistry is not usually markedly altered. The serum bilirubin is moderately elevated, and there is an immediate indirect Van den Berg reaction. In mild cases it averages 1–4 mg./100 cc., and in more severe cases 10–20 mg./100 cc. Hemoglobinemia has been detected in severe hemolysis. Blood cholesterol may or may not be elevated, though fat metabolism is usually normal as is protein metabolism. Iron elimination, however, is considerably increased.

Urine is usually dark, but contains no bile (acholuric jaundice) except during liver crises. Urobilin and urobilinogen are constantly present.

Pathology of the recticulo-endothelial system is quite characteristic, particularly that of the spleen which, according to Thompson, is constant and diagnostic of familial or spherocytic jaundice. It is usually large weighing between one and two kilograms. The weight in our Rh negative case was 2.9 kilograms. This, we believe, to be the heaviest spleen reported for this disease. The capsule is usually somewhat thickened, but adhesions are rare except over infarcted areas. The cut surface is dark red and convex, bulging above the capsule. The framework of the spleen is not maintained, and malpighian bodies are not seen grossly, but on microscopic examination are small and normal in number in proportion to the splenic size. The pulp is characteristically engorged by red cells so that the pulp cells are scant, and there is no noticeable increase in connective tissue framework.

The venous sinuses are markedly dilated and lined by two or three layers of large endothelial cells. Although there is no general increase in iron pigment, iron incrustation within the trabeculae is not infrequent and siderofibrotic nodules are occasionally seen. There is no definite evidence of phagocytosis.

Other tissues of reticulo-endothelial composition show evidence of pigment deposition. The bone marrow is red and hyperplastic with numerous normoblasts and myelocytes. Ectopic myeloid tissue is sometimes encountered along the vertebral bodies. The liver is occasionally cirrhotic probably due to liver damage brought about through previous episodes of marked anemia and anoxemia.

PATHOGENESIS

The pathogenesis of this disease is still a much discussed topic, and therefore the various theories will only be alluded to briefly. The fundamental fault is increased blood destruction either through exaggerated normal processes of blood destruction or through wholly abnormal processes. The normal process in the spleen is fundamentally fragmentation supplemented by the action of

certain cells in the spleen and other parts of the body in further breaking down corpuscular fragments.[1] However, erythrophagocytosis and hemolysis have never been demonstrated in the normal process. Therefore, in abnormal blood destruction several possibilities appear. The cells may be more fragile than normal, the blood serum may contain destructive agents, or erythrophagocytosis may be present.[1]

Thompson believes that increased fragility is the only deviation from normal necessary to produce the disease, and that spherocytes are formed by abnormal erythropoiesis. Dameshek and Schwartz, however, show evidence that the microspherocytosis is just one of the steps in the process of hemolysis. They also bring forth the argument that microblasts and reticulated microcytes are infrequently found in the peripheral blood and bone marrow in this disease. Overproduction of hemolysins or underproduction of anti-hemolysins, both of which are found in balance in normal serum, may result in free hemolysin. In other abnormal blood states, auto-agglutinins, auto-hemolysins, isohemolysins have been found, and it is conceivable these may be the cause of the hemolysis in this disease.

Dameshek and Miller believe that hemolysis is an active process due to red cell injury by a variety of agents, such as, pure hemolysins, complex hemolysins, or agglutinins.[7] Spherocytosis, as seen in this disease, indicated incomplete hemolysis by means of the activity of some hemolytic agent, but which may not be readily identified. This spherocyte then, they state, may become completely hemolyzed by erythrostasis which therefore is only of secondary importance to the primary action of the hemolysin.

The part that the spleen plays in this disease has always been of some debate. Is it primarily the site of the abnormal blood destruction, or is it only an accessory to an otherwise stimulated hyperfunction elsewhere? Dameshek and Miller feel that the spleen is more than simply an organ of stasis, but may have an active hemolytic function as well, particularly in acquired hemolytic anemia. We must not lose sight of the fact that it does take an active part in the normal process of blood destruction, that in familial hemolytic jaundice it undergoes marked hyperplasia as well as hypertrophy, and that improvement follows splenectomy in the typical familial case.

THERAPY

The treatment of the disease is not an emergency for, as it has been noted, the symptoms of the disease are not distressing except in crises. The duration of life is not shortened nor are the patients incapacitated, except during crises, or because of a large abdominal tumor; although the latter usually in itself is not troublesome except from the cosmetic standpoint. The studies of this family, as well as other family groups made in the Abington Memorial Hospital,[8] suggest that perhaps we should be bolder in advising surgical treatment with a view of preventing crises.

It has long been thought that transfusions were of great benefit in hemolytic anemias, particularly in sickle cell and Lederer's acute secondary hemo-

lytic anemia. They have been used for a long time as one of the most important parts of the therapy of congenital hemolytic icterus, but many clinicians advise against their use in this disease as they may be the trigger mechanism in setting off an acute crisis, and may even prove fatal if given during a crisis. Farr has reported such a case in which the clinical condition was aggravated by transfusion—showing moderate liver degeneration with recovery following splenectomy. This suggests that an acute liver failure is one of the pathogenic mechanisms of the clinical crises observed in the hemolytic anemia. Lowe[4] has demonstrated quite accurately that during a crisis, a form of acute hepatitis frequently occurs with diminished liver function, as demonstrated by liver function tests and pigment conversion and excretion. In one such episode, the patient was transfused and appeared to improve, but in another attack no transfusion was given and improvement was just as dramatic and rapid.

TABLE II

B. P., Rh negative patient, 2/4/46
Coag. time, 5½ min.
Bleeding time, 2½ min.
Platelets, 328,000
Fragility hemolysis begins
0.46% completed, 0.32% NaCl
Hemoglobin, 15.5 Gm. 102%
Red count, 4,970,000
White count, 9,000
Polys, 60
Lymphs, 37
Monocytes, 3
Prothrombin, 65%
Icterus index, 6
Van den Bergh direct delayed.
indirect 0.6

D. H., sister, 2/4/46
Coag. time, 6 min.
Bleeding time, 1 min.
Platelets, 409,000
Fragility hemolysis begins,
0.44% completed, 0.32% NaCl
Hemoglobin, 100%
Red count, 5,100,000
White count, 7,400,000
Polys, 66
Lymphs, 30
Monocytes, 4
Prothrombin, 80%
Icterus index, 5
Van den Bergh direct delayed.
indirect, 0.5

C. P., father, 2/4/46
Coag. time, 5 min.
Bleeding time, 1½ min.
Platelets, 307,000
Fragility hemolysis begins,
0.44% completed, 0.32% NaCl
Hemoglobin, 14.2 Gm. 92%
Red count, 4,620,000
White count, 8,400
Polys, 63
Lymphs, 35
Monocytes, 2
Prothrombin, 60%
Icterus index, 6
Van den Bergh direct delayed,
indirect, 0.6

It may then be stated that transfusing during a hemolytic crisis shows a preliminary decrease in blood destruction, but followed by a definite increase, and therefore an increase in clinical symptoms. The spleen and liver become large and more tender, and pigment production increases markedly. Bone marrow function is likewise suppressed, as evidenced by a drop in red cells, nucleated red cells, hemoglobin and reticulocytes.[4] These findings are substantiated by like findings in our series.

The only effective treatment is splenectomy which is usually followed by the disappearance of all symptoms. It has been stated that the signs of the disease, spherocytosis and increased fragility, persist indefinitely after splenectomy. However, the serum bilirubin and urobilin excretion becomes normal and the anemia definitely improves. The follow-up blood studies on three of the members of this family, taken a year or more after operation, are shown in Table II.

These essentially normal findings, along with blood studies made on nine other patients from one to three years after splenectomy for this disease, lead us to take exception to the above statement that severe spherocytosis and increased fragility persist indefinitely after splenectomy.

Operation is usually contraindicated during an acute hemolytic crisis, but may be undertaken in the course of an unusually prolonged or severe exacerbation of hemolytic activity, if the diagnosis is accurate. Our operative mortality for splenectomy in this disease during the past five years in the Pfeiffer Surgical Clinic for 21 cases has been zero.

During an acute attack, plasma infusions are the only form of approved therapy, blood being contraindicated in many cases due to the presence of agglutinin—agglutinogen reactions. Operative procedures during these attacks should only be attempted if other complications arise such as uncontrollable hemorrhage or dangerously progressive hemolysis.

CASE REPORT

B. P., a 21-year-old white female, presented herself for admission to the Abington Memorial Hospital on November 14, 1944 with the chief complaints of abdominal mass, malaise, occasional nausea, and chills and fever.

History of Present Illness. Patient has had an enlarged abdominal tumor, presumably spleen, since birth, at which time she was quite jaundiced. Patient experiences no pain or discomfort from the abdominal tumor except for small food capacity. She has episodes about two months apart of severe jaundice with malaise and vomiting productive of sour bile tinged material. Her skin has always been a trifle icteric.

Systemic Review. Gastro-intestinal—Avoidance of fatty foods, but no actual qualitative dyspepsia. Good appetite but small capacity.

Genito-urinary—Menses have always been irregular with quite severe dysmenorrhea. No urinary symptoms.

Cardio-respiratory—Dyspnea on exertion. Frequent colds.

Neuromuscular—Negative.

Past Medical History. Except for the usual childhood diseases, the past history was negative except for one rather significant fact, *i.e.,* in her early teens she had a sinus drainage at which time she received her first transfusion and suffered a rather severe reaction with chills and fever.

Family History. Father and paternal grandfather have splenomegaly with exacerbations of jaundice accompanied by abdominal pain. Father's sister and two of her four children are similarly affected. Patient's sister has mild splenomegaly. Family on mother's side gives no history of the disease.

Physical Examination. T—100, P—84, R—20 on admission.

Examination revealed nothing of note other than that of the skin and abdomen.

The skin was of a distinct icteric sallow appearance. The right ankle presented on the external malleolus, a chronic ulcer of four years duration which was about 6 x 6 cm., mildly tender at the periphery, and at times spontaneously productive of pain.

The liver edge extended approximately three fingers below the right costal margin. The left abdomen from the costal margin and the lateral border of the erector spinae down to the iliac crest was completely filled with a large firm mass which crossed the mid-line into the right abdominal fossa at the level of the iliac crest, moving freely on respiration, and which was tender only on firm pressure.

Clinical Impressions. The history of long standing jaundice, the splenomegaly and hepatomegaly, the exacerbations of jaundice associated with severe abdominal pain, nausea, and chills and fever, and the apparent high familial incidence of jaundice, and the

splenomegaly on her father's side, led us to make the tentative diagnosis of acute familial hemolytic icterus.

Clinical Progress While in Hospital. Nov. 14:—Admitted with red cell count of 2,690,000; hemoglobin of 6.9 Gm. 44 per cent.

Blood type A, not typed for the Rh factor.

Nov. 16:—500 cc. of compatible blood. Not crossed for Rh factor.

Nov. 17:—Menstrual period started with moderate dysmenorrhea.

Temperature spiked to 103° and was suggestive of transfusion reaction. Typed for Rh and found to be Rh negative, a fact that should have been suspected from the history of having had a severe reaction following a transfusion in childhood.

Hemoglobin was 3.8 Gm. 24 per cent, and red cell count, 1,670,000.

Icterus index 24, Van den Bergh indirect 2.5, direct delayed.

Fragility hemolysis begins 0.80 per cent completed 0.50 per cent.

Nov. 19:—Patient was assumed to be in an acute hemolytic crisis. She complained of some nausea and abdominal pain with chills and fever ranging between 99° and 103.°

RBC of 1,510,000, hgb. 2.9 Gm. 19 per cent.

500 cc. of plasma given.

Nov. 21:—Temperature still spiking. Urine urobilinogen qualitatively and quantitatively positive, 1:50 dilution. 500 cc. plasma given. It was decided to give patient test of blood; 100 cc. of compatible whole blood Rh negative type O was started intravenously. Only 50 cc. given because of marked reaction with chills and fever to 103° F. Van den Bergh taken before blood was given revealed delayed direct and indirect of 2 mg. Test taken three hours after 50 cc. whole blood, revealed delayed direct and indirect of 3 mg. This 1 mg. rise was sufficient to indicate increased hemolysis.

Nov. 22:—500 cc. plasma given. Hbg. 3.6 Gm. 23 per cent, RBC 1,460,000. Reticulocyte count 3.4 per cent. Prothrombin 60 per cent.

Nov. 31:—Temperature subnormal last four days. Now ranging between 98° and 100° F.

Dec. 1:—Splenectomy.

Operative Report. On December 1, 1944, under general anesthesia, the patient was operated upon by Dr. J. Walter Levering. A left pararectus muscle displacement incision was made, displacing the rectus muscle medially. The peritoneal cavity was opened and the spleen, approximately 15 inches in length came into view immediately beneath the peritoneum. Its surface was smooth, glistening and of a greyish hue. The intestines were then packed out of the way, and the hilus of the spleen identified. Because of the size of the spleen it was impossible to turn it medially; although there were no dense adhesions. A large rubber intestinal clamp was then placed about what was believed to be the primary spleen pedicle. The pedicle was then clamped by means of several Kelly clamps adjacent to the splenic tissue and distal to the rubber intestinal clamp. It was then divided between the Kellys. Dissection thus far had been comparatively bloodless, however, at this time on attempting to mobilize the spleen more fully and to identify the remaining vessels, an extremely large vein was unavoidably torn. The presence of the intestinal clamp, however, prevented retraction, and the bleeding vein was immediately visualized and clamped. The spleen was then delivered from the abdominal cavity in toto. Further examination of the abdominal cavity at the site of removal revealed two small marble-like accessory spleens, these were removed. It is interesting to note three other gland-like structures adjacent to the large vessels were ligated at their pedicles along with the clamped pedicle of the primary spleen. Examination of the diaphragm and splenic site revealed a smooth peritoneal surface which was completely free of any bleeding.

The gallbladder was then examined and found to be approximately four inches in length, the fundus blue and slightly distended. However, the neck and the proximal 2/3 were opaque and yellow. A large stone was palpable at the neck of the gallbladder. It was felt, however, inadvisable to attempt further surgery at this time. The abdominal

cavity was closed in layers without drainage. The sponge and pack count were correct. Clips were used to close the skin. A large compression bandage and scultetus binders were placed on the abdomen to attempt to restore preoperative intra-abdominal tension.

Pathologic Reports. Specimen consists of a tremendously enlarged spleen measuring 30 x 16 x 9 cm. and weighing 2,950 Gm. The surface is smooth and a dull slate grey color. On section considerable blood oozes from the surface which is dark brownish red homogeneous color. Scattered within the substance are numerous pinhead sized glistening opaque white nodules. On a number of transverse sections nothing further is found which differs from the description of the cut surface.

Microscopic: The splenic pulp is tremendously engorged, and the sinusoids are dilated and filled with red cells and hemosiderin. There is surprisingly little fibrosis. The malpighian follicles are large and have prominent central secondary follicles. There is no evidence of neoplasm or inflammation (Fig. 1).

Report of Gland-Like Accessory Structures. Gross: The specimens consist of two smooth-walled bluish red nodules measuring 12 x 9 x 7 mm. and 10 x 8 x 8 mm. respectively. The former nodule has rather a homogeneous nature and is more suggestive of lymphoid tissue than splenic. The other nodule on section shows a homogeneous dark red substance with a few tiny opaque pinhead sized nodules throughout. This nodule is more suggestive of accessory splenic tissue. One must conclude from the above report that it is difficult to differentiate at operation between an enlarged lymph node and an accessory spleen.

Microscopic Section shows one nodule to be lymph node, showing a little hyperplasia and the other a small nodule of accessory splenic tissue.

FIG. 1.—Spleen of B. P. RH negative case. Weight 2,950 Gm.

Post-Operative Course: Pre-op:—RBC 2,620,000, hbg. 7.1 Gm. 46 per cent.

Post-op: Immediately: RBC 3,320,000, hbg. 9.5 Gm. 60 per cent.

It was felt that this great rise in red cell count and in hemoglobin was due to hemoconcentration.

Dec. 2:—Temperature began to rise last night reaching 102° at 9:30 P.M. RBC 3,260,000, hbg. 9.5 Gm. 61 per cent. 500 cc. plasma and intravenous fluids given daily. Patient placed in oxygen tent.

Dec. 3:—Temperature reached 103.6° at 4 P.M. and rapidly fell towards normal.

Dec. 4 to Dec. 7:—Patient has run slightly elevated temperature and has experienced some chest pain. X-ray revealed a left plural effusion, but no lung pathology. RBC averaged about 2,780,000. Hbg. averaged about 7.8 Gm. 50 per cent.

Dec. 11:—Patient was progressing very well, had no transfusions of whole blood but receiving only plasma and infusions. Hoping that we might establish an allergic reaction intradermal injection of Rh+ blood (citrated) was tried, but it gave no sensitivity reaction. Controls run with Rh— blood and with citrate in normal saline.

Dec. 23:—Patient discharged from hospital feeling quite well, but still running slightly elevated temperature.

RBC 2,860,000, hbg. 6.6 Gm. 43 per cent. Reticulocytes 0.2 per cent.

As an outpatient, patient appeared for tri-monthly laboratory studies check-up. Seemed to gain strength and weight.

On May 13, 1946, patient returned to the hospital with symptoms suggesting an attack of acute appendicitis. The following day cholecystectomy and appendectomy was done by Doctor Levering. A distended gallbladder with a stone in the cystic duct was removed, as was an acute catarrhal appendix. Thorough search failed to show any accessory spleen. Patient made an uneventful recovery, and was discharged two weeks after admission.

Follow-up studies gave evidence of continued marked improvement following splenectomy. When last seen in February 1947, she was actively working as a waitress. She was very healthy, and even the ulcer on her right ankle that she had had for four years previous to the splenectomy had completely disappeared. Her last blood study, as noted on Chart I, was entirely normal.

BRIEF RECORD OF SISTER AND FATHER OPERATED UPON DURING THE SAME PERIOD

Sister. March 5, 1945, D. H., 25-year-old white female, admitted to hospital with the chief complaint of large abdominal tumor of 20–23 years duration and occasional attacks of abdominal pain and jaundice. Patient is now three and one-half months pregnant.

Past Medical History. Scarlet fever, tonsillectomy, adenoidectomy, and mastoidectomy as a child. Appendectomy performed five years ago, one week after which patient developed jaundice. Patient has had one child followed by puerperal convulsion.

Family History. This case is the sister of B. P., Rh negative.

Physical Examination. Spleen palpable in left upper quadrant and extending down to level of umbilicus. Uterus palpable two fingers above symphysis pubis. Other findings negative.

Laboratory Data. Patient presented an anemia of 2,100,000 RBC's and 8 Gm. or 52 per cent hemoglobin. Fragility hemolysis begins 0.50 per cent completed 0.36 per cent NaCl. Reticulocyte count was 7.0 per cent on admission, but rapidly was reduced postoperatively to 0.4 per cent 13 days post-operative. Indirect Van den Bergh was 2.8 mg. on admission but dropped to less than 0.4 mg. before discharge. Blood indices on admission were: Volume per cent 28. Mean Corp. Vol. 101. Mean Corp. Hemoglobin 32.6. Mean Corpuscular hemoglobin concentration 31.4. Volume index 1.15, Color index 1.10. Saturation index 0.89. On day of discharge, March 21, 1945, the patient's hemoglobin was 11.8 Gm. or 77 per cent, and reticulocytes 0.4 per cent.

Friedman test on admission was positive.

Operative Report. Operation performed on March 7, 1945, by Doctor Levering, revealed a moderately enlarged spleen and liver, and a markedly diseased gallbladder containing numerous stones. A routine splenectomy and cholecystectomy was performed and patient's convalescence was uneventful. Patient discharged March 21, 1945.

Pathologic Report. Gallbladder showed infiltration by bile pigment and presented metabolic cholelithiasis.

Spleen showed a picture of congenital hemolytic icterus and weighed 473 Gm.

The patient's follow-up was uneventful and she delivered a normal child at term. The last follow-up blood count is shown on Chart I.

Father. On February 4, 1945, C. P., male, 45, white, the father of the two preceding cases, was operated upon in the Jewish Hospital, Philadelphia.

Laboratory Findings. Platelets 253,820. RBC fragility began 0.5 per cent completed 0.3 per cent. Blood sugar 93 mg. Blood urea nitrogen 18 mg. Blood count: hemoglobin 14.5; RBC 5,180,000, WBC 10,900, neutrophiles 67 per cent, lymphs 29 per cent, eds. 1 per cent; monos 2 per cent; 1 per cent bas.

Operative Report. The patient operated upon under fractional spinal anesthesia. The spleen was removed, and weighed 515 Gm. He had an uneventful recovery and his follow-up blood studies, taken about a year later, are shown on Chart II.

CHART I

SUMMARY OF SIGNIFICANT LABORATORY DATA

		Admission	Case B .P.—R. H;								
						⌐— 12/1/44 —¬					
	Normals	11/14/44	11/18/44	11/24/44	11/27/44	Pre-op.	Post-op.	12/4/44	12/21/44	1/12/45	3/19/45
Hbg. Gms. and percent	13.7–17 85–105%	6.9 44%	2.9 18%	4.5 29%	5.1 33%	7.1 46%	9.5 61%	8.5 55%	6.6 43%	71%	11.9 77%
RBC's (thousands)	4,500–5,500	2,690	1,510	1,940	2,240	2,620	3,100	2,780	2,860		
WBC	6,000–8,000	8,200	2,500	7,000	6,400	6,100	13,200	10,200			
Mat neuts	50–70%	63	72	77	79	80	87	91			
Lymphocytes	20–25	30	26	23	20	17	12	7			
Monocytes	4–8	7	2		1	3		2			
Nucleated reds	0		2	1							
Reticulocytes	Less than 1%		3.4%	3.2%	12.8%		9.8%	12.6%	0.2%		0.5%
Normoblasts	0										
Prothrombin	70–100%	50%	60%	55%	50%		35%	35%			
Platelets	200,000–400,000				191,000			254,000			
Wassermann	Negative	Neg.									
Kahn	Negative	Pos. 3+									
Kline	Negative	Pos. 2+									
Hematocrit	45%							31% vol.			40.5%
Mean cell vol.	87	83 cu. microns									104
Mean cell hbg.	29.5	26.9 micromicrograms									31.2

CHART I—*Continued*

SUMMARY OF SIGNIFICANT LABORATORY DATA

Case B. P.—R. H.

	Normals	Admission 11/14/44	11/18/44	11/24/44	11/27/44	12/1/44 Pre-op.	12/1/44 Post-op.	12/4/44	12/21/44	1/12/45	3/19/45
Mean cell hbg. conc.	35	32									
Mean cell diameter	7.7	6.2 m.									7.0
Mean cell thickness	1.95	2.80 m.									
Vol. index	1.00	0.95									
Color index	1.00	0.94									
Saturation index	1.00	0.91									
Vol. thickness index	1.00	1.80									
Diameter to thickness ratio	7.7:1.95 or 4:1	6.2:2.8 or 2.2:1									
Fragility—Begins	.44%	.80									0.46
Complete	.32%	.50									0.32
BUN	9–18	15						21			
Plasma NaCl	570–600	610						570			
Plasma CO_2	50–70	50						45			
Sugar vein	60–90	73									
total protein	6.5–8.0		5.41	6.21	6.45			6.28			
Cholesterol	125–300				184						
Icter. index	2–4	24	24	20							
Van den Bergh	Less than 0.4	Direct	Delayed 2.5 mg.								Direct neg.
Stool		Delayed ind. 2 mg.	Bile—neg.								Ind. less than 0.4 mg.

SUMMARY

A review of the symptomatology, the laboratory findings, the pathogenesis, and the therapy for familial hemolytic anemia is discussed. An unusual case of the disease, which was complicated by the Rh factor, is presented in detail. Two other cases in the same family are presented in brief. The follow-up blood studies showing normal figures are presented.

CONCLUSION

The Rh negative case report is of interest because of the complication which arose from blood transfusion.

The giving of plasma rather than whole blood not only in this case, but in other cases is recommended. Plasma infusions will supply the much needed electrolytes, and will elevate the low blood plasma which is present in these cases without the danger of increasing hemolysis.

The tremendous size of the spleen, 2950 Gm., of the Rh negative case is of interest. The recommendation of splenectomy, not only as a beneficial therapy, but also as a curative measure, is recommended.

The follow-up blood studies in our series suggest that splenectomy is not only beneficial in relieving symptoms, but is also curative in these cases of familial hemolytic anemia.

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ON THE SPECIFIC ROLE OF THE LIVER IN HEMORRHAGIC SHOCK*†

Report of Progress to Date

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THE CENTRAL DISTURBANCE in traumatic shock, regardless of the nature of the etiologic agent, is a rapid and progressive decline in the velocity of blood flow and a progressive trapping of blood[1, 2] throughout the general capillary bed with a resulting venous anoxemia and a concomitant widespread tissue anoxia. As shock continues, the time arrives when all known therapeutic measures produce no more than a transient, if any, favorable response. When this state of "irreversibility" arrives, the adverse effects of persistent and increasing tissue anoxia become rapidly cumulative with resulting early death.

This statement of the situation is not intended to ignore other factors which, if present, may contribute to the disorganization of the body economy, such as gross distortions in fluid and electrolyte balance and damage to specific organs or tissues by specific shock-inducing agents. These are complications that may modify but do not basically affect the primary characteristics of the shock phenomenon.

The tissues which are of vital importance to the co-ordinated activity of bodily processes essential to survival for even a brief interval (minutes to hours) are the central nervous system, the heart, the lungs, and the liver. Total failure of every other organ or tissue except these, in the present state of knowledge, would still permit integrated function consistent with survival over a period of many hours to days. The solution of the problem of such a rapidly lethal phenomenon as the irreversible shock state represents might be approached by considering the disturbances in these vital organs.

1. THE CENTRAL NERVOUS SYSTEM

The vasomotor system has been shown by the earliest workers in the field to be intact until the prelethal phase of shock. (The loss of vasomotion in advanced shock, demonstrated by Chambers and his collaborators,[3] is explained on a humoral basis.) Swingle *et al*[4] revived the theory that nociceptive stimuli from the area of injury induce or intensify shock because spinal anesthesia reduces the incidence of shock from muscle trauma to a lower extremity.

* Part of the work described in this paper was done under a contract, recommended by the Committee on Medical Research of the Office of Naval Research of the United States Navy and Harvard University.

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Wang[5] has recently shown a slightly greater tolerance to trauma by denervation of the traumatized extremity. The protective effect of spinal anesthesia, according to Phemister and his co-workers[6] is due to the decreased bleeding consequent to the reduction in blood pressure, while no protection is provided by section of the cord, the nerve roots or all the peripheral nerves to the extremity. Prolonged hypotension induced by stimulation of the cardioaortic nerves produces eventual exhaustion of the vasomotor center, but rapid recovery follows removal of the stimulation at any time before collapse of the vasomotor center. Stimulation of somatic nerves does not produce nerogenic shock. Phemister[7] summarized his work by stating that the neurogenic factor is of little or no importance except that hemorrhagic shock may be intensified by direct nerve stimulation sufficient to produce depression of the vasomotor center.

In hemorrhagic shock the key metabolites involved in biological energy transformations show very little disturbance in brain tissue in contrast to severe depletion of such substances in liver and kidney.[8] Consistent with these findings is the absence of significant signs of brain damage in dogs whose livers have been perfused throughout a prolonged period of hemorrhagic shock and in dogs which have recovered from "irreversible" shock as a result of perfusion of the liver (See below).

There is little or no direct evidence from the foregoing data to incriminate the nervous system in the development of the irreversible phase of shock.

2. THE HEART

Cardiac output is much reduced and continues to decline as shock reaches its terminal phase. There is a critical level of cardiac output which, if lowered even slightly by a small withdrawal of blood, results in sudden death. Since temporary improvement in cardiac output always occurs in response to repeated transfusions until just before death, the progressive decline in cardiac output would seem not to be due primarily to functional collapse of the heart. The myocardial weakness demonstrated by Werle, Cosby and Wiggers,[9] and by Kohlsteadt and Page,[10] and by Wiggers[11] is an expected result of prolonged anoxia, which affects the function of all tissues adversely. No bacterial or other toxin directly affecting cardiac function has been demonstrated to operate in hemorrhagic shock. Since a primary disorder in the central circulation has not been shown to exist,[12, 13] the cause of the progressive decompensation in the peripheral circulation must be sought elsewhere.

3. THE LUNGS

The lungs may be excluded from consideration because they continue to function adequately (as indicated by full oxygen saturation of the arterial blood until death), except when pulmonary edema results from overtreatment with fluids. Respiratory disturbances are generally due to reflex, metabolic and humoral factors.

4. THE LIVER

The extensive biochemical disturbances in shock[14, 15] may result from damage to cellular function in general or from a functional disorder in one or more organs of controlling importance in preserving metabolic equilibrium. There is reason to believe that a biochemical lesion in the liver is responsible for the rapid deterioration of the shock state.*

Thus the greater resistance to traumatic shock in rats fed a balanced diet as compared to rats on a low protein diet[17] may be correlated with the better respiration of liver slices from prefed rats in hemorrhagic shock than the respiration of liver slices from fasted rats in hemorrhagic shock.[18] LePage demonstrated in traumatic shock marked depletion of high energy phosphate substances in the hepatic and renal cells in contrast to slight depletion of these substances in other tissues.[8, 19]

If damage to the liver can be shown to be extensive enough, the rapid downhill course of the shock state might be explained on this basis alone. The liver receives some three-fourths of its blood supply from the portal vein. This blood, though venous, has an oxygen saturation value of some 15 volumes per cent. In shock this value is 5 per cent or less. Moreover, the volume flow through the portal vein and hepatic artery is greatly diminished. It is clear that great injury to liver function will result if this situation persists for very long.

There is an abundance of data to show that the liver suffers severe injury in traumatic shock. The secretion of bile slows up or stops and along with it bromsulphthalein clearance and other excretory liver functions must do the same.[20] The production of fibrinogen[21] and hypertensinogen[16] is reduced. Deamination in the liver is said to be deficient,[22] although the evidence is not unequivocal.[23] An ordinarily well tolerated withdrawal of plasma, if repeated in the same animal after the liver has been slightly injured, will result in rapidly fatal shock, while severe cell injury to other organs (kidney, pancreas, intestine) does not modify the response.[24] Finally, the friable, congested and discolored state of the liver at death from shock suggests not only the possible total absence of liver function but also the presence of toxic decomposition products.

These data indicate that liver injury may be specifically related to the development of that degree of functional deterioration which nullifies the effectiveness of any known therapeutic methods. Experiments to be described below were devised to test the validity of this hypothesis.

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* Damage to other organs such as the kidney or adrenal is not of such central importance because, in respect of metabolic effects, the loss of function in these organs is lethal only after several days.

The pressor response of the kidney to ischemia is lost early in shock. This does not implicate the kidney in the genesis of irreversibility because (1) bilateral nephrectomy does not alter the course of the shock state if it is induced before the damage from retention products occurs; (2) even if renin secretion could continue during shock, it would exert no benefit because of the early disappearance of hypertensinogen from the blood.[16]

SUMMARY OF DATA ALREADY REPORTED

If the liver of a dog in hemorrhagic shock is continuously perfused from the onset of the shock state by cross-circulation with a healthy donor animal, the development of irreversibility to transfusion is prevented and recovery from shock occurs.[25] The donor dog is apparently unharmed.

The cross-circulation set-up consists in a flow of arterial blood from a major artery of the donor into the splenic vein of the recipient (dog in shock) at a rate sufficient to approximate the normal total blood flow through the recipient's liver. The same volume of blood returns via both femoral arteries of the recipient to the systemic veins of the donor.

If this set-up is arranged so that the blood flow from the donor enters the recipient's systemic veins instead of the splenic vein, the course of the shock state is precisely the same as if no perfusion had been performed: i.e., irreversibility to transfusion is not prevented, all the manifestations of rapid and progressive decline appear and death follows, after the usual interval. In this case, too, the donor animal fully recovers and is virtually unharmed at the end of the experiment. It appears then that perfusion of the liver with arterial blood from a donor protects the liver against damage, while the remainder of the organism is subject to all factors of extrahepatic origin that might be contributing to the development of irreversibility to transfusion. To determine the extent to which any such factors might be involved, a second series of experiments were performed in which irreversibility was allowed to develop and the cross-circulation procedure was begun only after the therapeutic transfusion was observed to have failed.[26] In this second series the results were precisely the same as in the first. Perfusion *via* the splenic vein results in recovery: "taking-up"[25] disappears, blood pressure gradually returns to normal and all signs of a restored peripheral circulation become manifest. Perfusion *via* a systemic vein produces no noticeable improvement and death occurs as rapidly as if no perfusion had been carried out. *It follows that the liver can be repaired even after it has suffered extensive damage and that it is the organ directly responsible for failure of the peripheral circulatory apparatus in shock.*

The therapeutic objective in irreversible shock then requires (1) a determination of the mechanism operating between the liver and the peripheral circulatory apparatus and (2) a closer analysis of the nature of the contribution by the donor animal.

In respect to the first of these objectives we may postulate (a) the elaboration by the damaged liver of a toxin capable of paralyzing vascular tone or (b) the existence of a hormonal product of hepatic origin, normally available for the maintenance of vascular tone which, like hypertensinogen and fibrinogen, disappears as the hepatic cells become increasingly incompetent. No evidence for the latter is yet available.

That toxins can induce shock or increase susceptibility to shock is a well-recognized clinical fact, e.g., as in the case of infection. Are there any endogenous toxins in shock in which an infectious process can be safely excluded?

Chambers and his collaborators[27] suggested the presence of a circulating toxin in hemorrhagic and tourniquet shock. Callicrein, which occurs in animal tissues, produces shock when injected in concentrated form.[28] But its spontaneous appearance in the blood during shock cannot be demonstrated. Prinzmetal and Bergman[29] believe that a toxin is present in the blood of rats immediately after producing a hot water burn. Shorr *et al.*[17] developed the hypothesis that shock is due to an endogenous vasodepressor toxin by demonstrating a vasodepressor principle (VDM) in ice-cold saline washings of liver from the dog in hemorrhagic shock. Less is found in hepatic vein blood, still less in striated muscle and none elsewhere. This toxin of hepatic origin produces a transient shock-like state of peripheral flow in the mesentery of the test rat. If enough can be produced to permit testing its capacity to induce the shock state and to carry the latter to its lethal termination, stronger evidence of its specific etiology in shock would then be provided. We have reservations concerning the specific relation of this toxin to the shock state because it has not been found in dogs which were not under the influence of barbiturates. It is our view that the barbiturates intensify the shock state and so complicate the findings. Blood samples taken from our shocked animals (in which we used morphine only) and assayed for toxin in Shorr's laboratory did not show any parallelism between the clinical state of the animal and the toxin assay.[30] These tests, however, are yet in the exploratory stage. If a toxin is responsible for the lethal outcome of the shock state, it is difficult in our experiments to account for the healthy state of the donor animal when the recipient dies in shock. One must then assume a neutralizing function in the donor which is not available to the recipient in spite of a free intermixture of the two blood streams.

If the donor cures the recipient by neutralizing a toxin which acts on the peripheral vascular musculature, the same service should be available to the recipient regardless of the route of cross-circulation. Shorr states that the toxin from the shocked dog's liver is also formed by anoxic liver *in vitro* and is inactivated by healthy liver tissue. The toxin stops being elaborated if the anoxic liver is restored to an aerobic environment within a few hours. Since the donor makes a therapeutic contribution only because his arterial blood reaches the liver of the recipient directly, the donor's blood achieves its effect at least in large part by restoring an aerobic environment to the liver, rather than by the neutralization of a circulating toxin.

WORK IN PROGRESS*

The nature of the donor's contribution accordingly requires further analysis. This contribution might consist: (1) solely in a flow of arterial blood to the liver to supplement the deficient volume of oxygenated blood which the animal itself is supplying or (2) in an essential biologic substance no longer elaborated by the dog in shock. It is also possible that both are needed to

* Recent experiments were done with the assistance of Dr. E. D. Frank and Dr. L. H. Manheimer.

facilitate regeneration of that liver function which is essential for sustaining peripheral vascular tone or if a toxin is involved, to inhibit toxin formation.

An initial step in the solution of this problem was made by perfusing the liver of the dog in shock by a supplemental arterial supply from its own femoral artery instead of from a donor animal.[31] The volume flow from the femoral artery to the splenic vein nearly equaled the volume flow that was supplied by a donor animal. In a series of 15 such autoperfusion experiments the course of the shock state was definitely altered in that the rate of "taking-up" was reduced and survival of the animal prolonged, but recovery from the shock state was not effected, except in one instance. The evidence indicates that supplementary portal flow of normally oxygenated blood was not the sole contribution of the donor animal.

A series of liver perfusion experiments, in which a variable capacity pump supplied with a reservoir of fresh blood is used in place of the donor animal, is now being conducted. From the evidence to date, which is still preliminary, it appears that this will also fail to effect recovery and that the donor animal seems to make a biological contribution in addition to that of merely supplying arterial blood to the liver. For example, the donor supplies glucose, because the recipient's blood glucose level is maintained when cross-circulated with a healthy dog but not when autoperfusion is performed. If glucose is added to the autoperfusion circuit, the blood glucose level may be maintained. In any case, the addition of glucose does not alter the final result. What other substances the donor's blood provides which the recipient's own blood does not, remains to be determined.

In another series of experiments now in progress, liver perfusion from the shocked dog's own femoral artery is accompanied by cross-circulation between the donor and the systemic veins of the shocked dog. To date, the results of this study indicate that the benefit conferred does not equal that of direct liver perfusion. The possible adverse effect of the additional A-V shunt created will require further evaluation.

A complicating factor of serious import in many of these experiments is the development of intraperitoneal bleeding of massive proportions, which results in loss of the animal before the result can be evaluated. This bleeding is not due in most instances to technical errors or local trauma. It is an expression of the shock phenomenon and deserves intensive investigation, since it is an even grosser manifestation of tissue disintegration than the more familiar one of hemorrhagic extravasation into the gut.

We observed long ago that bleeding into the intestine in hemorrhagic shock is mild or insignificant until the irreversible stage is reached and then occurs only if transfusions are given. It is a striking fact that liver perfusion from a donor reduces this complication, whereas other types of perfusion do not. By the use of silicone-lined tubing we have been able to reduce the amount of heparin needed in these experiments to a trace, but without completely eliminating the intraperitoneal bleeding, particularly in dogs who have been allowed to deteriorate too extensively. Therefore, although we may be able to omit

heparin entirely in future cross-circulation experiments, we cannot expect to avoid this complication. Meanwhile, in an attempt to explain the bleeding we have made the following observations: (1) the prothrombin time increases only slightly in advanced shock; (2) the coagulation time is not altered; (3) fibrinogen is not produced by the liver during shock, but some remains in the blood and more is added from transfused blood. Consequently, the hemorrhage is presumably not due to gross defects in the coagulation process; (4) the portal venous pressure is substantially elevated in shock after transfusion (even without added inflow from an arterial anastomosis).[32] The range of elevation is sufficient to produce hemorrhagic extravasation into the gut and the peritoneal cavity.[31] To what extent the hemoperitoneum is a manifestation of the failure of liver recovery or merely an unrelated complication which prevents recovery that might otherwise occur, remains to be determined.

SUMMARY

Cross-circulation of the liver of the dog in hemorrhagic shock with a healthy donor animal is the only effective therapeutic agent so far known for the treatment of hemorrhagic shock irreversible to transfusion. The nature of the donor's contribution consists in something in addition to merely oxygenated blood flowing into the liver. At present the problem is to determine what this additional service is.

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THE REDISTRIBUTION OF BODY WATER AND THE FLUID THERAPY OF THE BURNED PATIENT**†

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As knowledge of the physiologic alterations peculiar to the burned patient has unfolded in the past two decades, the concept of plasma volume deficit has become firmly entrenched as the central feature.[1, 2, 3] Restoration of this volume towards normal, or prevention of its diminution, has become the prime objective of fluid therapy. But burned patients still succumb to their injuries, and the frontier of survival has not been pushed very far back despite isolated reports of the survival of remarkably extensive burns.[4] Apparently, there are still aspects of the disordered physiology of burns which we do not understand well enough to treat effectively. The disordered fluid balance of burn shock may be confused by the presence of pulmonary damage or infection, by widespread physiologic changes due to the trauma, or to misdirected treatment.

During a period of enthusiasm in the field of burn therapy, ranging from treatment with large quantities of sodium ion to massive whole blood transfusion, we have planned a study based not on theory but on observation of the physiologic variables. The present paper deals with the disorders of fluid distribution encountered in 19 patients. New concepts of guiding the fluid therapy of the extensively burned patient have emerged.

METHODS

Measurement of the Body Fluid Spaces

Plasma volume has been measured by the dilution of Evans blue dye, as described by Gibson and Evelyn.[5] In the study of burns several considerations are pertinent to this method. A clear serum is necessary for colorimetry and cannot always be obtained. Hemoglobin and bilirubin may both be present in the early phases. Standard correction for these substances has not yielded satisfactory results in our hands. During the period of maximal nutritional deficit and forced feeding, the 8- to 12-hour fast required for clear sera is not always advisable.*

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* The use of the dye method of measuring plasma volume in burns has a theoretic inaccuracy which has been discussed elsewhere.[6] The increased capillary permeability of the burn wound permits equilibration of the dye with a larger volume of fluid outside the capillary wall; but such equilibration requires time. Practically, we have found by checking the dye method with the radioactive red cell volume[7] that if two readings are made after injection of the dye, the first at 10 and the second at 30 to 50 minutes after injection, the determination is still valid even in the extensively burned patient.

Normal values for the plasma volume (PV) are variable and occupy a range from 3.5 to 5.0 per cent of body weight, the latter figure being exceptional and found only in large healthy males of athletic habitus. For the average patient 3.5 to 4.5 per cent of body weight is a normal range; it will be noted that this involves a 30 per cent variation from the lower figure.

Red cell volume has been measured by calculation from the dye plasma volume and the large vessel hematocrit, and by the dilution of red cells containing radioactive iron, a method which is independent of hematocrit differences in various areas of the vascular bed. The radioactive method has been described by Gibson *et al*,[8, 9] and the results in our patients are reported in the paper dealing with the anemia of burns.[7]

Extracellular fluid volume has been measured by the dilution of thiocyanate[10, 11] and of radiosodium[12] using the plasma concentration at 50 minutes after injection. The latter method is perhaps the more physiologic though they both readily reveal extracellular fluid expansion or contraction and in their similarity and occasional variance have yielded much data of interest in these patients. (In the tables the plasma, thiocyanate and radiosodium volumes are designated by PV, SCNV, and NA*V respectively.)

Our experience in measuring the body fluid spaces coincides with that of others in finding a wide variation in normal values for plasma volume, red cell volume and blood volume; furthermore, modes of expression such as "per cent of body weight," "cubic centimeters per kilogram," "liters per square meter," "cubic centimeter per centimeter of sitting height" and other more complex measurements yield little increase in accuracy or predictability.[13, 14, 15] For our purposes, "per cent of body weight" seems most practical, and normal values are as follows:

Plasma Volume	3.5 — 4.5 % BW	(= Body Weight)
Dye Red Cell Volume	3.0 — 4.0 % BW	
Radioactive Red Cell Volume	2.6 — 3.5 % BW	
Thiocyanate Space	18.0 — 25.0 % BW	
Sodium Space	18.0 — 25.0 % BW	

Measurement of External Wound Loss

By measuring the amount of sodium in the exudate, the external water loss from the wound may be calculated. The calculation is based on the assumption that sodium leaves the wound in the concentration found in plasma, a reasonable assumption since this concentration is found in bleb fluid. Methods based on the weight of dressings suffer from loss by evaporation; the nitrogen content is a poor guide to water content as the breakdown of protein to non-protein-nitrogen and the evolution of ammonia by bacterial putrefaction affect both calculation and result.

By calculations from water intake and output, with estimates of insensible water loss and measurements of extracellular space expansion, the water loss

through the wound may be further approximated. For example, if in a four-day period a patient is given 20,000 cc. of water, and excretes 4,000 cc., undergoes an extracellular expansion of 5,000 cc. and loses by lungs 1,000 cc. a day for a total of 4,000 cc. then:

$$20{,}000 - [4{,}000 + 5{,}000 + (4 \times 1{,}000)] = 7{,}000 \text{ cc.}$$

The 7,000 cc. represent unaccounted for water loss and must have been either stored in cells or lost via exudate.

Measurement of hourly urine output has been most helpful clinically in controlling therapy and casts considerable light on the renal mechanism in burns. This method will be described in detail later in this paper.

Measurement of red cell, electrolyte and protein concentrations in the blood have been carried out as a reference point for other calculations.

Measurement of electrolyte and protein balances, including exudate losses, have been an integral part of the study and are described in a subsequent paper.[16]

OBSERVATIONS

The objective of the studies recorded in this paper has been a comprehensive plan for the fluid therapy of the extensively burned patient. The appraisal of the plan of therapy has depended not so much upon survival of the patient as upon the values obtained in a series of coordinated laboratory measurements. The maintenance of an adequate circulation has been judged not only by continuous measurement of the renal excretion of water and electrolytes but also by repeated direct determinations of the plasma and red cell volumes. The demands of the wound have been gauged by measuring both the expansion of the interstitial fluid space and the fluid, electrolyte and protein losses from the wound surface. The subsequent fate of the huge amounts of fluid given as therapy and pocketed as edema has also been studied by continuing the laboratory observations throughout the period of resorption of the wound edema. From the balance sheet the true needs of the patient have been reconstructed.

Observations have also been made of the size of the fluid spaces in healthy human beings under normal and induced circumstances and in patients with diseases either akin to burns or requiring therapy commonly employed in burned patients. Space does not permit inclusion of these control studies.

BURNED PATIENTS

Of the 19 patients included in this study, 16 had extensive skin burns, covering from 25 to 85 per cent of the body surface; five of these patients died. The 17th patient had a burn of 15 per cent and the 18th and 19th burns of only 5 and 4 per cent. The 19th also had a pulmonary burn.

It was obviously necessary to have a plan of therapy with which to initiate the study, one elastic enough to be altered as knowledge was gained. Formulas for estimating the fluid requirements of a burned patient based upon the degree

of hemoconcentration had been recommended at the beginning of World War II. The hemoglobin concentration or hematocrit of peripheral blood was used to determine the degree of hemoconcentration.[17, 18, 19] For each degree of hemoconcentration present a certain volume of fluid was recommended as therapy. Adequate to restore to normal the volume of plasma circulating at the time the measurement was made, these formulas failed to take into account the volume of plasma fluid which was to be lost from the circulation in the hours after the particular hemoglobin or hematocrit reading had been made. Thus an extensively burned patient, seen within a half hour after injury when the hemoconcentration had had little time to advance, would be given a small quantity of fluid whereas in reality such a patient requires many liters of fluid in the first 12 hours in order to avoid circulatory insufficiency.

It was considered that a sounder prediction of the fluid requirement of the burned patient could be made on the basis of the extent of the surface area damaged.* The reasoning took into account not only that the volume of plasma water lost from the damaged capillaries into the wound is proportional to the area of skin surface burned rather than to the depth of injury but also that planning of therapy for an entire 24- or 48-hour period was in order regardless of the degree of hemoconcentration at the particular moment the patient was seen.[20, 21]

Part of the program on burns undertaken at the Massachusetts General Hospital for the OSRD, was a study of the advantages and shortcomings of administering fluid in accordance with the extent of surface area damaged. The following formula for this relationship, based on experience with extensively burned patients treated in 1942–43, was adopted for trial.[22]

Surface Area Formula for Fluid Therapy

The surface area formula for fluid therapy of burned patients is based upon the concepts that the demands of the wound are proportionate to its extent, that the rate of edema formation will decrease with time after injury and that the requirements of normal metabolism including kidney function, must be met in addition to those of the wound. In the average sized adult for each 1 per cent of the body surface burned, 75 cc. of plasma and 75 cc. of non-colloid-containing isotonic electrolyte fluid are given in the first 24 hours. These fluids are to fill the expanding spaces of the wound and to keep up with any seepage of the

* At a conference on burns called by the National Research Council on January 7, 1942, under the chairmanship of Dr. I. S. Ravdin, it was agreed that a surface area formula should be recommended to the Armed Services. This was the first time that the extent of the surface area burned was to be a major guide to the therapy of burn shock. Drawing on his experience with the hemoconcentration formulas and the surface area as a first-aid fluid formula, Dr. Henry N. Harkins calculated that patients with 10 per cent or more of their body surface burned should be given 1,000 cc. of plasma intravenously in the first 24 hours for each 10 per cent of the surface burned. The conference recommended that salt solution, not to exceed the same quantity, should also be given. The formulas tested by us have been modifications of this recommendation.

wound surface. The quantity of non-colloid electrolyte solution equal to the amount of plasma is planned because measurement of the fluid in burn blebs suggests that wound fluid has a protein concentration a half to two-thirds that of normal plasma but a pattern and concentration of electrolyte essentially that of plasma. The electrolyte solution is to be given by mouth to those patients who are not nauseated; otherwise it is given intravenously along with the plasma. The intravenous route is considered less desirable since it is theoretically possible that the more prompt dilution of the protein of the circulation occasioned by the intravenous injection accelerates capillary filtration and edema formation in the wound. For the oral administration, an isotonic solution of sodium was prepared with one-third of the sodium as bicarbonate and two-thirds as chloride; it was flavored with fruit syrup. For the intravenous administration, the physiologic sodium chloride solution available to the armed forces was used, recognizing that the chloride concentration was in excess of that in the extracellular fluid and that it might produce high chloride concentrations in the plasma.

One-half of the calculated amount of plasma and electrolyte fluid is given in the first eight hours and the second half in the subsequent 16 hours, in this fashion adapting the rate of the therapy to the expected rate of transudation into the wound. Both the experimental[23] and clinical observations carried out at this hospital suggest that the rate of edema formation follows a parabolic curve, rapid at the beginning, tapering off as wound pressure increases, with cessation of further edema formation around the 36th hour. In keeping with this decreasing rate of edema formation, the plan includes for the second 24 hours a fluid ration equal to one-half that given in the first 24 hours.

In addition to the above, 2,000 cc. of fluid is given in each 24-hour period to maintain urine flow. (Insensible water loss and the water resulting from metabolism were not specifically considered.) The fluid is given preferably by mouth and consists of palatable liquids; those containing sugar and potassium, such as fresh fruit juices, being offered freely. If the fluid has to be given intravenously, glucose in water is used. The volumes of each of these three fluids are subject to alteration according to the exigencies of the case, the continued presence of hemoconcentration or cessation of renal output indicating the need for accelerated intake.*

Wound Edema—Expansion and Contraction of Interstitial Space

The volume of wound edema, the rate of edema formation and its subsequent subsidence have been measured in 14 patients.** The volume of wound

* It should not be construed in the application of the formulas described in this paper that whole blood transfusion is contraindicated. The need for whole blood is discussed in the paper dealing with the anemia of thermal burns.[7]

** The edema observed was not due to lack of pressure dressings. To all burns of the head and extremities dressings of bulky, compressible cotton were applied and held firmly in place by elastic gauze bandages. The pressure thus afforded reduced the edema locally but displaced it proximally. The effect of pressure dressings and their limitation in sparing plasma loss are discussed elsewhere.[24]

edema equals the increase in volume of the interstitial space over normal, the interstitial space being the extracellular fluid volume minus the plasma volume. Previous clinical observation of visible burn wounds not covered by bandages, such as those of the face, suggested that maximal edema in the human being is reached between the 36th and 48th hours and that in burns of partial thickness, the subsidence of the edema may be almost as rapid after the 48th hour as its formation. Care was therefore taken to make as many determinations of the extracellular space as practicable within the first few days, with always one determination close to the 48th hour. In this manner it was possible to test the clinical impression and determine the maximal volume and the rates of edema formation and disappearance. The results are divided according to both the extent and the depth of injury. Differences in value were found between the thiocyanate and radioactive sodium ion determinations in some patients during the phase of edema formation and during subsidence of edema in patients with extensive deep septic wounds. The data are given in Tables I-X. The relation of maximum edema reached as the result of the burn trauma to the extent of injury is depicted in Chart 1.

Circumscribed Burns. Fluid space measurements were carried out in two patients with circumscribed burns:

Case 264.*—A 41-year-old woman was admitted immediately after receiving circumscribed partial thickness burns of the arms, 5.5 per cent in extent.** The interstitial space increased not more than one liter in volume; the variations both in thiocyanate and radiosodium volumes are within those inherent in the methods (Table I, Chart 1). The plasma volume during the period of maximum edema was at the lower level of the normal range for women (slightly lower than that for men). The patient received no specific fluid therapy for her burns because of their limited extent. She showed no clinical evidence of systemic disturbance.

Case 205.—In contrast to the findings in the previous case are those in a man of 56 years of age, with partial thickness skin burns of even lesser extent (4 per cent), limited to hands and face, but who also had a pulmonary tract burn from the inhalation of hot oil. The interstitial space expanded 7 liters in the first 48 hours (Table II, Chart 1). This expansion, out of proportion to the area of skin damaged and more like that encountered in the extensively burned, is believed due to the combination of the position of the skin burns which resulted in a greater spread of subcutaneous edema and of the pulmonary damage.

The interstitial space did not retract to normal until after the third week. On the 14th day the patient's plasma volume was excessive; a phlebotomy was followed promptly by clinical relief. This enlargement of both portions of the extracellular space is believed related to over-enthusiastic fluid therapy initiated after the 36th hour as well as to the pulmonary damage of which there were continuing signs and roentgenographic evidence.

* The same case numbers are used in all articles on burn patients studied at this hospital under contract with the Committee on Medical Research. Numbers 1 through 39 refer to the Cocoanut Grove fire cases; numbers 40 through 96 to cases studied before the Cocoanut Grove fire; and numbers 97 through 282 to cases studied since the Cocoanut Grove fire.

** Extent of the burn, total, partial, and full thickness, is always expressed as per cent of the body surface in the papers of this series. The per cent is computed according to the Berkow scale.[25]

TABLE I

PLASMA AND EXTRACELLULAR FLUID DATA

Case 264

Female, Age 41, Weight 52.5 Kg.

Extent of Burn: 5.5 percent total, 0 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc.	% BW	cc.	% BW	cc.	% BW
2	1740	3.33	9,020	17.3	10,900	20.9
3	1790	3.42	11,700	22.4	10,790	20.6
8	....	....	10,300	19.8	11,900	22.7

TABLE II

PLASMA AND EXTRACELLULAR FLUID DATA

Case 205

Male, Age 56, Weight 79. Kg.

Extent of Burn: 4 percent total, 0 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc.	% BW	cc.	% BW	cc	% BW
0(4.5 hrs.)	2760	3.50	14,850	19.0	15,590	19.6
1					19,950	25.2
2					21,900	27.8
3					19,600	25.0
7	2720	3.45	21,500	27.2	22,300	28.4
9	3290	4.30	24,730	31.2	18,320	23.0
14	4250	5.30	19,400	24.5	.....	....
17					19,900	25.0
20	3670	4.65	23,270	29.2	20,000	25.3
26			17,260	21.8	18,200	23.0

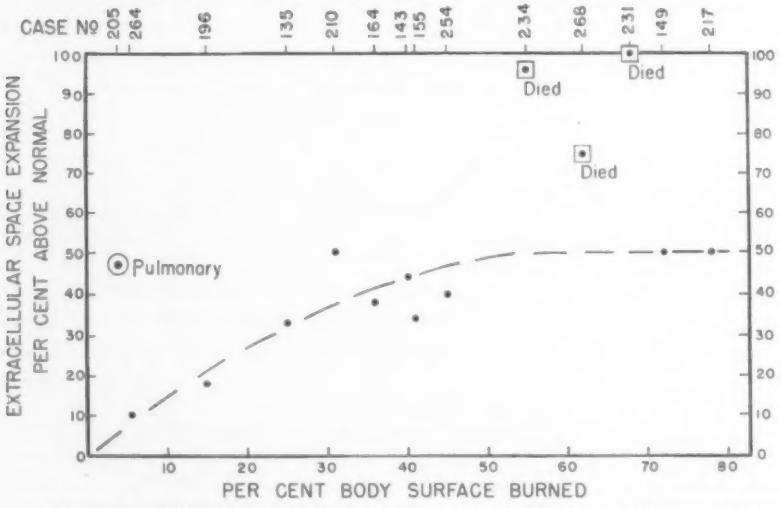

CHART 1.—Relation of Extent of Burn to Expansion of Extracellular Space and Need for Fluid Therapy.

The extent of the burn wound in per cent of body surface damaged is plotted against the expansion of the extracellular space in per cent above the normal volume. The observation recorded is the maximum found from the 36th to 72nd hour in each of 14 patients.

The patient to whom each observation pertains is identified by the case number at the top of the chart. Three of the patients died (Cases 234, 268 and 231); the expansion was 75 per cent or greater. Of the 11 patients who survived, including the two most extensively burned, none had an expansion greater than 50 per cent. One of the survivors (Case 205) had an expansion out of proportion to the extent of the skin burn (4 per cent); he had inhaled hot oil.

Extensive Burns. The expansion and contraction of wound edema were studied in 12 extensively burned patients. In eight the fluid therapy is considered to have been adequate, in two it was excessive; one of the patients succumbed. In the remaining two, it is probable that poor kidneys and infection rather than excessive therapy produced an inordinate expansion of the interstitial space and eventual death.

Of the eight patients receiving adequate but not excessive therapy, five are considered together because they were consecutively treated patients with extensive full thickness burns upon whom comparable studies were made.

Cases 135, 143, 149, 155, 164. The measurement of the dye plasma and thiocyanate volumes were planned with the specific purpose of plotting both the rates of edema formation and retraction. Multiple measurements were made in the first seven days and occasionally thereafter. The data are summarized in Table III and Charts 2a, b and c. (See also Chart 1).

The patients were fully grown, their ages varying from 16 to 48 years. In Table III, Column 3, it is seen that the burns ranged in extent from 25 to 72 per cent. The extent of full thickness destruction was also variable, from 7 to 38 per cent. Column 5 indicates that immediately following admission the patients showed hemoconcentration both of cells and protein. In Column 9 are shown the increases found in the thiocyanate space. The increases average 8 per cent of the patient's body weight, varying from 7 to 11 per cent. These increases represent expansions of 35 to 55 per cent over the normal extracellular volume. In Column 10 it will be noted that the total therapy administered to the patients in the first 48 hours averaged 328 cc. per per cent of burn. Of the figures in this Table, the deviation from the average is the least and for the reason that the therapy given each patient was almost exactly that outlined by the surface area formula. For anyone not familiar with the treatment of burns, this amount of fluid may seem remarkably large.

In Column 11 it will be noted that the plasma given in the first 48 hours averaged 92 cc. per 1 per cent burn. The amount of plasma given per per cent of burn varied more than did the total amount of fluid. The amount outlined in the formula is 110.5 cc. per per cent burned and it was exceeded only in the most extensively burned patient. In the others when the plasma ran slowly through the needle, the deficit was replaced by salt solution.

In Column 12 it will be noted that, with the exception of the most extensively burned patient, the thiocyanate space expansion was slightly larger than the amount of plasma given.

Column 13 indicates that the urinary volume in all of the patients was adequate and approached an excessive amount in only one, Case 143.

The importance of renal function as an indication of the state of the circulation and of hydration is illustrated by the following experience with Case 149, the most extensively burned. An inlying catheter had been secured in the patient's bladder at the time of entry to the hospital and the urinary output was carefully observed. In the 7th hour after injury the flow of urine ceased. A second intravenous needle was inserted and plasma was pumped by syringe into

TABLE III

SUMMARY OF BODY FLUID MEASUREMENTS AND EARLY THERAPY IN FIVE SEVERELY BURNED PATIENTS

1	2	3	4	5		6		7		8		9		10	
Pts.	Wt.	Percent Burn	Admission Hours Post-Burn	Hemoconcentration Maximum Hematocrit and Protein		Admission PV		Admission SCNV		48-Hour SCNV		To SCNV Increase		Total Therapy 1st 48 Hrs.	
No.	Kg.	Total/Full Thickness	Hrs.	Percent Cells	Gm./100 cc.	cc.	% BW	cc.	% BW	cc.	% BW	cc.	% BW	cc.	cc./%
135	53.0	25/15	5.0	50.0	7.2	1880	3.55	10,800	20.4	14,100	26.7	3300	6.7	8,600	342.0
143	58.7	40/34	1.0	56.4	6.6			(Footnote 1)		16,900	29.0	5300	9.0	12,000	300.0
149	66.1	72/38	1.5	70.0	7.5	1940	2.90	15,200	23.0	22,660	34.0	7460	11.0	21,375	295.0
155	78.2	41/26	4.0	58.0	7.1			(Footnote 1)		20,970	27.0	5460	7.0	16,100	394.0
164	71.2	36/7	0.5	50.7	7.2	2840	4.00	18,790[2]	26.4[2]	19,070	27.8	5550[3]	7.8[3]	11,107	309.0
Averages				57.0	7.1					18,740	28.7	5414	8.3	13,836	328.0

11		12	13	14	
Total Plasma 1st 48 Hrs.		Plasma Given SCNV Expansion	Urine Output 1st 48 Hrs.	Calculated External Water Loss[4] 1st 48 Hrs.	
cc.	cc./%	Ratio	cc.	cc.	cc./%
2250	90.0	0.682	1440	1860	74.5
4250	106.0	0.800	5900	0	0
9250	129.0	1.270	4450	7465	103.7
3250	79.2	0.592	3370	5270	128.5
2071	57.5	0.370	4110	0	0
4214	92.3	0.743	3854		
			160 cc./hr.		

[1] These determinations could not be completed because of extensive hemolysis producing free serum hemoglobin.

[2] This thiocyanate volume was not done on admission, but was done about three hours after admission, after treatment had been under way for about two hours. It therefore represents a considerably expanded value over normal.

[3] This calculation of increase in thiocyanate space is based on an increase over the normal estimated value for this patient rather than an increase over his first observed thiocyanate volume.

[4] Calculation of external water loss: Ext. Loss = Total Therapy—(SCNV Expansion + Urine + 2000 Insensible Loss).

both veins, 750 cc. of plasma being injected in the space of 20 minutes. Ten minutes after the start of this accelerated plasma injection, urine once more dripped from the catheter. An hematocrit taken at the start of the accelerated injection proved to be 70 per cent, and that an hour later was 63 per cent. Had the catheter not been in place, the cessation of renal function and the circulatory insufficiency producing it, would certainly not have been so promptly recognized. Although the period of anoxia necessary to damage the kidney has not been established with certainty in the human being,[26] it is probable that had the deficient circulation to the kidney persisted for a matter of hours, sufficient renal damage would have accrued to jeopardize the survival of the patient. This episode dramatically illustrates the usefulness of a close observation of renal output in managing fluid therapy in the early phase of an extensively burned patient. Only by dint of this rapid massive therapy was a fatal outcome avoided and when the opportunity to mobilize his edema arrived he excreted 20,000 cc. of urine in four days (second to sixth days). A young male, he was able to excrete this large amount of water, whereas an older patient might not have been able to do so and would have been more prone to develop visceral and pulmonary edema during resorption. Since the treatment administered was barely enough to avoid serious hemoconcentration, the edema and subsequent diuresis cannot be regarded as due to over-zealous treatment.

In Column 14 it will be observed that the calculated external water loss is extremely variable. Though it is accepted that some patients with dry, charred, parchment-like burns may have little or no external water loss in the first 48 hours (Case 143 had burns of such character), this was not so true of Case 164. One cannot, therefore, accept the zero figures as absolute, but rather as a general indication that external water loss was minor. In patients 155 and 149, external water loss was large by this type of derived calculation; both patients had large areas of moist wounds.

The rate of edema formation is illustrated in Chart 2a. The figures charted are the per cent deviation from the normal thiocyanate space; since the variations of plasma volume were inconsequential, the changes depicted represent changes in the interstitial space. The increase in volume of the interstitial space is rapid in the first 48 hours, the maximum volume measured in four patients being between the 40th and 50th hours. In three of these patients the next measurement, made between the 5th and 6th days and before any operation, showed the volume to have decreased (Cases 135, 143 and 149). In the 4th (Case 155), the volume remained unchanged on the 5th day; because of the appearance of respiratory difficulty it is believed he may have been given an excess of fluid. The one patient whose interstitial fluid volume increased significantly after the 48th hour was Case 164. The measurement was made on the 7th day, two days after an excision and grafting operation; the red cell mass of 1,210 cc. measured at the same time indicated a severe anemia. This continued increase in interstitial fluid volume doubtless had a complex origin and is presumably not a primary result of the burn. Observations on the control patients indicate that the operation and severe red cell depletion should be

associated with an increase; wound infection known to be present also presumably played a role.

In summary, the findings depicted in Chart 2a indicate that the expansion of the interstitial space due to burn trauma occurs rapidly, reaching a maximum within 48 hours. Other factors such as wound infection, operation, anemia and excessive fluid therapy may influence the degree of expansion and time of onset of retraction.

Charts 2b and c depict the variations encountered in concentration in the peripheral venous blood of protein and red cells in terms of the per cent deviation from normal. Of the protein there is an initial increase in concentration, the explanation of which is discussed in the paper on the shift of protein.[27] This increase is inversely proportional to the concentration of protein in the burn edema fluid. The increase is followed by a dilution with eventual return to normal with healing of the wounds. The extent and duration of the dilution

CHART 2a

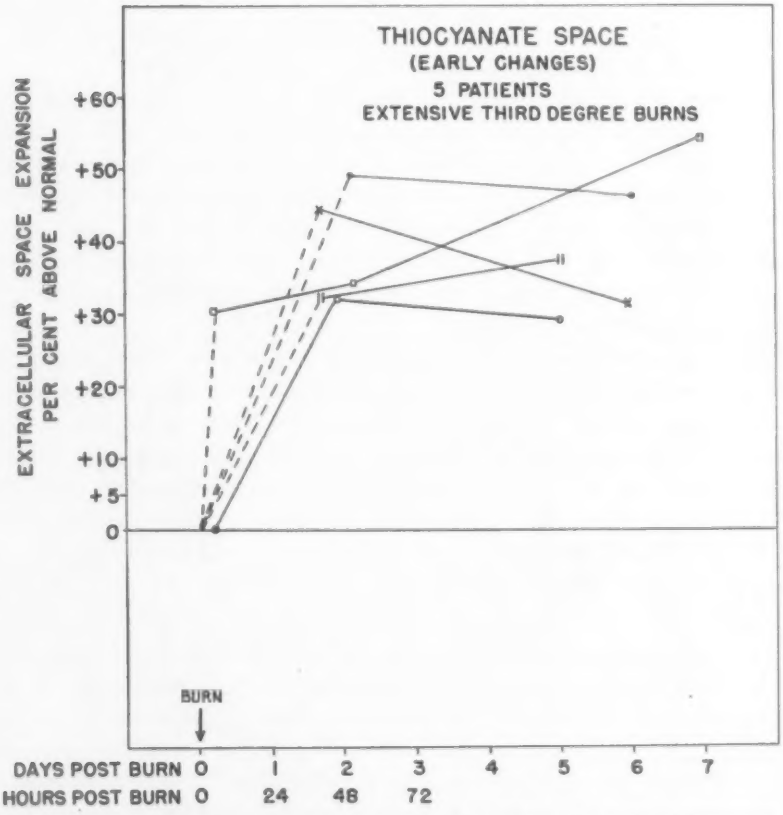

CHART 2a, b and c.—Three charts demonstrating the early thiocyanate space changes and alterations in peripheral concentration of protein and red cells in the five severely burned patients tabulated in Table III (Cases 135, 143, 149, 155 and 164). For discussion see text.

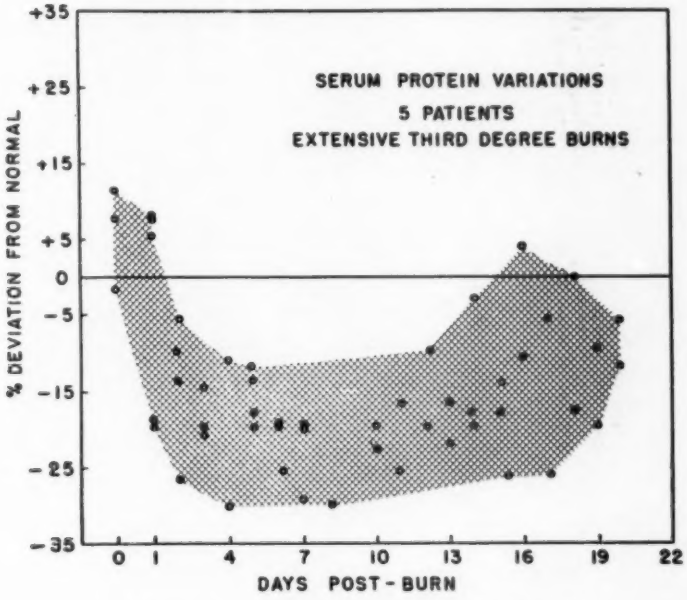

CHART 2b.—(See legend under Chart 2a.)

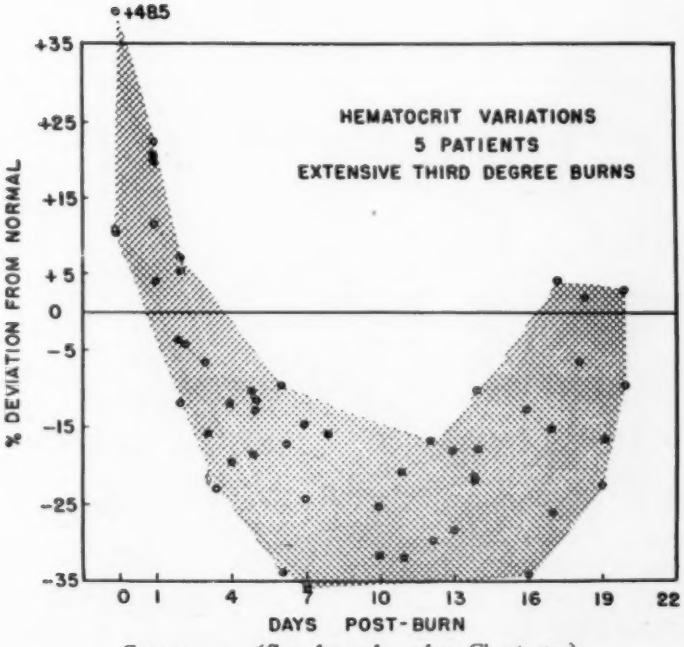

CHART 2c.—(See legend under Chart 2a.)

depends upon the osmotic balance left by fluid therapy, resorption of edema fluid, kidney function, protein destruction and synthesis.

The graph of the concentration of red cells (Chart 2c) follows a curve parallel to that of the protein, the initial concentration resulting from loss of plasma volume, and the subsequent dilution resulting more from diminution of red cell mass than from excessive plasma volume in these cases.[7]

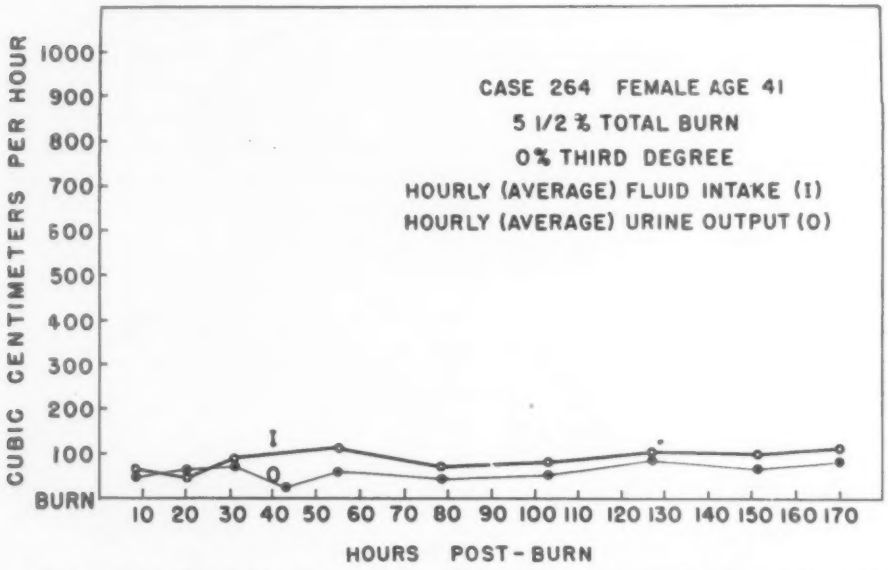

CHART 3.—Intake-Output Chart of a Patient with a Circumscribed Burn (Case 264). The intake-output charts are plotted similarly. The ordinate depicts the fluid intake or output rate in cubic centimeters per hour, the abscissa hours after the burn. Intake is indicated by I, output by O. Volumes indicated by points at 12- to 24-hour intervals are averages. The actual observed hourly renal outputs from an inlying catheter are indicated by multiple, closely spaced points.

In Chart 3 there is no significant spread between the intake and output over that which would be produced by ordinary insensible loss.

In subsequent charts, as the intake progressively rises over the output following more extensive burns, the area intervening between intake and output is a function of the water stored in the wound and lost through the dressing.

The deep wounds of the five patients were treated with early excision and grafting, the initial operation taking place between the 5th and 7th days. Although there was a diuresis after the 48th hour, the interstitial space expansion persisted and final retraction to normal did not occur until healing of the wounds was well advanced. The patients were discharged home from the 60th to 122nd post-burn day with wounds healed.

In the 6th extensively burned patient who received adequate therapy, the findings are much the same as in the previous five cases with the addition that the extracellular space was measured with radiosodium as well as thiocyanate.

Case 210.—A 34-year-old housewife was admitted shortly after receiving a 31 per cent total, 25 per cent full thickness burn. Her early course was marked by what was regarded

at that time as oliguria (see below); on her 6th day she had a saphenous vein ligation because of phlebitis following cannulation. On her 8th day she had an excision of a portion of her burns. These areas were partially grafted 11 days later; the patient had a long and difficult convalescence and was discharged home on the 128th post-burn day.

The observations made on this patient prove that the expansion of the interstitial space is obligate, not a result of therapy. On admission the patient showed a diminished plasma volume (Table IV) and this together with her high hematocrit and high protein concentration indicated the familiar early tendency to plasma loss and burn shock. An expansion of the extracellular space to 50 per cent above normal was observed.

The patient's initial treatment was not excessive and during the initial 48 hours the patient's urine output was at low but adequate levels, 1,470 cc. during the first 24 hours (an average of 61 cc. per hour) and 846 cc. during the second (an average of 35 cc. per

TABLE IV

PLASMA AND EXTRACELLULAR FLUID DATA

Case 210
Female, Age 34, Weight 73.0 Kg.
Extent of Burn: 31 percent total, 25 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc.	% BW	cc.	% BW	cc.	% BW
0 (2 hrs.)	1790	2.5	12,900	17.7	16,070	22.8
5	(1640)	2.3	22,200	30.5	21,600	29.6
8	3450	4.7	25,400	35.0	20,500	28.0
15	3330	4.6	20,300	28.0	19,600	27.0
24	2640	3.5	17,300	23.6		
32	2180	3.0	21,200	29.0	18,200	25.0
47	3040	4.2	21,200	29.0	17,900	24.5
61	3100	4.3	21,300	29.4	17,800	24.5
83	2620	3.6	16,900	23.1		
114	2460	3.4	20,400	27.8	18,500	25.3
127			17,500	24.0	16,900	23.2

hour). During the first 48 hours the patient received 11,253 cc. of fluid of which 4,020 cc. was plasma. According to the surface area formula described, her therapy for the first 48 hours was to have totaled 3,485 cc. of plasma, a like amount of non-colloid-containing electrolyte solution plus 4,000 cc. of fluids, a total of 10,970 cc. Although it is conceivable that her minimal requirement was less than given, this is unlikely in view of the continuing mild hemoconcentration and small urinary volume during the first 48 hours. It is of interest that the 8 liter expansion in extracellular fluid revealed by the second measurement (5 days post-burn) correlated so closely with the difference between intake and output during the first 48 hours, 8,937 cc. (Chart 1). In patients who are flooded with water one cannot estimate the volume of the burn edema by the volume of fluid retained because the factor of renal function looms so large and a discrepancy between intake and output may reflect renal damage.

After the first 2 days, the patient's fluid therapy was intensified because the urine output was not at that time regarded as adequate. The intensified therapy consisted of approximately 19,000 cc. of fluid during the next 3 days and the concomitant excretion of 12 liters of urine from the 3rd to 5th days, inclusively.

The remaining two of the eight patients with extensive burns receiving adequate therapy had burns of but partial thickness with only small areas of full thickness destruction.

Case 196.—A male, age 51, received a burn of 15 per cent total, 1 per cent full thickness. His fluid therapy was purposely delayed until the 6th hour to permit study of the differential sodium-thiocyanate expansion in an untreated burn. At the end of five hours the thiocyanate space was only slightly higher than normal, 22.6 per cent of his body weight, whereas the sodium space, at 29.4 per cent, had expanded significantly (Table V).

TABLE V

PLASMA AND EXTRACELLULAR FLUID DATA

Case 196
Male, Age 51, Weight 80 Kg.
Extent of Burn: 15 percent total, 1 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc.	% BW	cc.	% BW	cc.	% BW
0 (5 hrs.)	3500	4.38	18,200	22.6	23,700	29.4
3	....	....	18,600	23.5	.....	....
4	....	....	17,250	21.6	16,050	20.0
9	4560	5.60	16,800	21.0	18,250	22.6

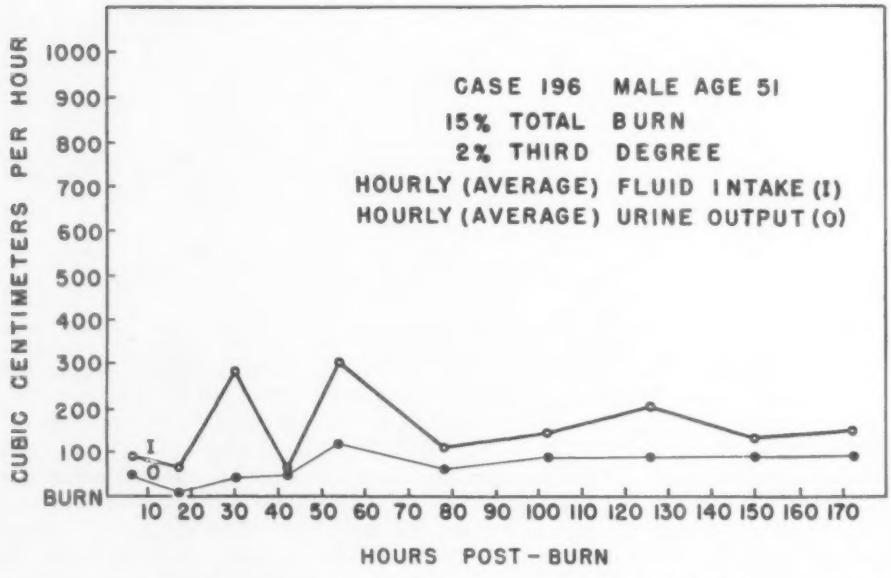

CHART 4.—Intake-Output Chart of a Patient with a Superficial Burn of 15 Per Cent and a Full Thickness Burn of but 2 Per Cent (Case 196).

In this patient, slightly more extensively burned than that of Chart 3, the intake departs from the output during the first 60 hours, indicating some storage of water in the wounds. The discrepancy is less than that found in more extensively burned patients.

This finding of a larger sodium space is of interest because it has been observed in other patients within the first days after injury. It indicates that the volume of fluid in which sodium is dissolved is greater than that into which the thiocyanate can pass. Normally the volumes receiving these two ions are equal. This finding in burned patients suggests that the sodium ion penetrates

cell barriers not open to the thiocyanate and may be due either to the trauma *per se* or to a generalized dehydration in the acute phase after injury. The more prolonged elevations of the thiocyanate space frequently observed in patients with a chronic open wound (when the sodium space may be normal or near normal) also indicate some difference in significance of the two methods.

Case 196 never approached shock and never showed evidence of serious fluid disorder. The fluid allotment provided by the surface area formula proved adequate (Chart 1). He developed considerable facial and head edema, but by the 3rd day after his burn when his sodium space had returned towards normal, the patient had mobilized and excreted his edema and was essentially

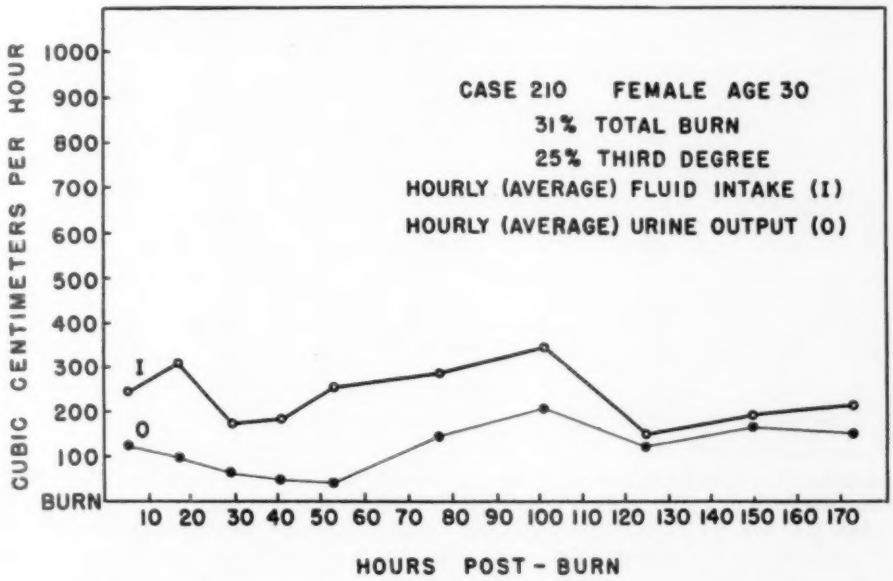

CHART 5.—Intake-Output Chart of a Patient with a 31 Per Cent Total Burn, Most of Which Was of Full Thickness Destruction (Case 210).

There is a prolonged discrepancy between intake and output which does not resolve itself until approximately 120 hours after the burn. During this time the patient was treated conservatively, at times her urine output being low. This may account for the prolonged period of intake-output discrepancy. The patient was slow to mobilize the edema fluid and did not show a clear-cut diuresis.

normal. His partial thickness burn healed with rapidity and he did not show the prolonged elevation of the thiocyanate space we have found associated with extensive, chronically infected, full thickness burn wounds. The changes indicate a need for water, electrolyte and protein adequate to meet the demands of the burn wound. These demands are transient as the tissues retain the viability essential to early recovery of capillary permeability and resorption, or mobilization, of the edema fluid.

This patient never demonstrated any hypoproteinemia; on two observations on his first post-burn day he showed slight hemoconcentration with respect to

red cells, presumably related to the accumulation of edema during that period and to the fact that treatment was purposely withheld for six hours to study the sodium-thiocyanate discrepancy.

Case 254.—A previously vigorous electric power linesman 38 years of age received an electric flash burn of 45 per cent, only 5 per cent being full thickness injury. Of note was the observation that the volume of his extracellular space when first measured was out of all proportion to the fluids which had been given him, and that he proved subsequently, nine months after the accident, to have an unprecedentedly large interstitial fluid volume as measured by dilution of the thiocyanate ion (Table VI).

According to the surface area formula, 3,375 cc. of plasma and 8,750 cc. of total fluids should have sufficed for his requirements for the first 24 hours. Because of continued

TABLE VI

PLASMA AND EXTRACELLULAR FLUID DATA

Case 254
Male, Age 38. Weight 68.8 Kg.
Extent of Burn: 45 percent total, 5 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc.	% BW	cc.	% BW	cc.	% BW
2	....	....	35,000	51.0	26,500	37.0
3	....	....	29,600	43.0		
4	....	....	30,600	44.5		
5	....	....	.....	....	27,700	40.0
7	4640	6.7	33,200	48.0		
11	4320	6.3	24,500	35.5	17,840	15.8
9 mos.	3540	5.2	25,400	36.5		

apparent hemoconcentration of mild degree, judged by an hematocrit above 45 and a serum protein concentration above 7.0 Gm./100 cc., this allotment was exceeded by 750 cc. of plasma and the total by nearly 3 liters of fluid in the first 24 hours. After his wounds were healed and he was clinically well, his hematocrit was found to be 47 per cent and serum protein 6.6 Gm./100 cc. In retrospect the fact that he secreted 2,538 cc. of urine in the initial 24 hours, approximately 1,300 cc. more than adequate, suggests that the urinary output would have been a wiser guide to the fluid therapy than the apparent hemoconcentration.

Measurement of the extracellular space by the thiocyanate method on the second day after the burn yielded a surprising volume equal to 51 per cent of the body weight. (The sodium space was significantly smaller.) Other patients showing a volume of such proportion were precariously ill and subsequently succumbed, yet this patient was clinically tolerating his injuries well. This paradox was explained when nine months later his extracellular fluid volume was found to be 36.5 per cent of his body weight. Such a large volume is unprecedented in our experience in an overtly healthy man, and remains unexplained.

If the volume of his extracellular fluid measured nine months post-burn is accepted as his normal, two concepts emerge which are useful in treating this type and size of burn. The increase in volume as a result of the burns found at 48 hours after burning, represents a 40 per cent increase in volume, not 150 per cent, above the normal (Chart 1); this change in volume in the first 48 hours would also represent a 10,000 cc. increase, a figure in keeping with the actual fluid balance (including a 750 cc. loss from the wound in the first 48

hours calculated from the sodium content of the exudate). A 40 per cent increase in extracellular volume is to be expected in patients with burns of this extent, comparable to the experience in patients with full thickness burns.

The second important finding is that the initially expanded interstitial space had retracted to normal by the 11th post-burn day. Such a prompt retraction is not seen in patients with extensive skin burns predominantly of full thickness destruction.

The experience with the two patients having extensive burns who received excessive fluid therapy and one of whom died is as follows:

Case 217.—A 26-year-old woman was brought to the hospital within an hour after receiving burns of 78 per cent, 45 per cent of the total surface being of full thickness destruction. Her first days were marked by intensive fluid therapy and massive edema.

TABLE VII

PLASMA AND EXTRACELLULAR FLUID DATA

Case 217
Female, Age 26, Weight 92.8 Kg.
Extent of Burn: 78 percent, 45 percent full thickness

Day Post-Burn	PV		SCNV		Na^*V		
	cc.	% BW	cc.	% BW	cc.	% BW	
0 (1 hr.)	2320	2.5	18,000	19.5	19,800	21.5	
1	....	....	23,300	25.2	25,450	27.5	
2	....	....	.....	....	28,000	30.5	
3	2890	3.1	27,500	30.0	22,800	24.7	
10	4080	4.4	27,400	30.0	.....	....	
24	4040	4.4	27,200	29.3	21,500	23.5	
48	3880	4.2	28,800	32.0	19,600	21.3	
68	3210	3.5	20,400	22.0	15,900	17.2	
95	2970	3.2	26,400	28.6	20,100	22.0	
13 mos.	2400	3.2	19,600	26.0			(Wt. 76 Kg.)

From the 4th to 10th days she exhibited an increasing fever. Because of this indication of acute infection, plans for early surgical care of her full thickness burns were abandoned. Her wounds healed by granulation, epithelization and grafting over a period of many months. She was discharged home on the 190th post-burn day.

The first determinations of the plasma volume and hematocrit made one hour after injury indicated that an uncompensated plasma loss had already occurred (Table VII). The extracellular measurements made at the same time were within the normal range and suggested that the uncompensated plasma deficit and wound edema had resulted in some dehydration of the rest of the body. As in other patients in the presence of dehydration, the radiosodium volume was larger than that of the thiocyanate.

Soon after therapy was begun the usual expansion of the interstitial space took place (Chart 1). By the 3rd post-burn day when the patient's clinical edema was beginning to subside, the sodium space receded back to 25 per cent of the patient's body weight and from then until healing the thiocyanate space remained expanded, the sodium space remaining more nearly normal. This continued enlargement of the thiocyanate space but not that of the sodium, is the characteristic finding during the convalescence of patients with an extensive infected open wound.

The patient's blood volume on the 3rd post-burn day was only 4.65 per cent of the body weight, one of the lowest total blood volumes we have observed in this group of cases and due unquestionably not only to the uncompensated plasma loss but also to massive destruction of red cells described in the report of the anemia of deep burns.[7]

In this patient, therapy based on the surface area formula would have resulted in the administration of 5,850 cc. of plasma, a like amount of non-colloid-containing electrolyte solution, plus 2,000 cc. of fluid, all in the first 24 hours. This schema was exceeded by 7,600 cc., for during the first 24 hours the patient received 21,313 cc. of treatment of which 6,240 cc. was plasma.

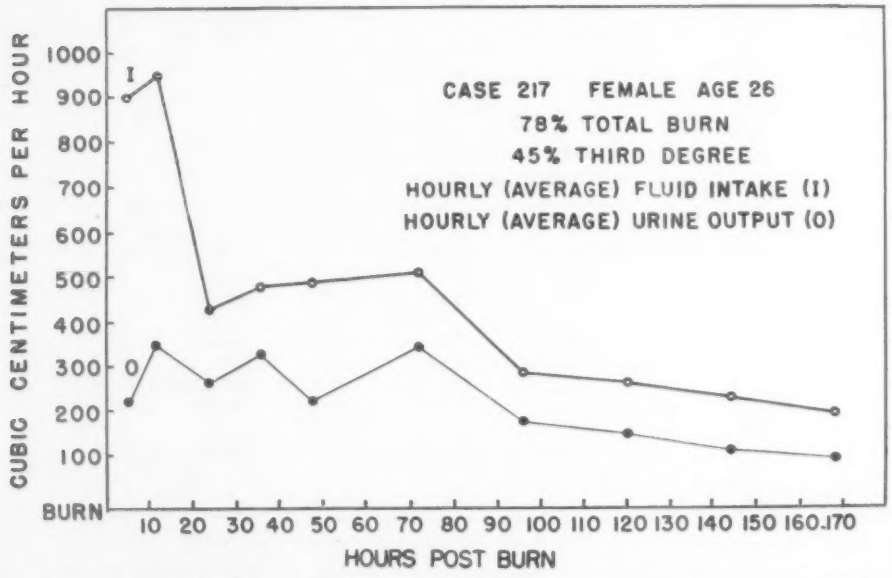

CHART 6.—Intake-Output Chart of an Extensively and Deeply Burned Patient Whose Initial Treatment was in Excess of that Necessary (Case 217).

There is a large discrepancy between intake and output during the first 24 hours when edema formation is most rapid. From the 100th hour on, a normal relationship is exhibited. The high average urine output during the first 80 hours, averaging around 300 cc. per hour, illustrates, in the light of subsequent experience, that fluid therapy was being administered at a rate more rapid than essential.

During this time the patient's urine output was 6,855 cc. with an added 1,000 cc. loss as vomitus. External losses arrived at by calculation were very severe amounting to somewhat over 5 liters during the first 48 hours.

This patient was treated with excessive zeal and the load placed on her kidneys thereby was tremendous. As it turned out, the volume of fluid indicated by the surface area formula should have proven adequate to the need; the forcing of the fluid intake might well have led to a fatality. During the patient's second 12 hours in the hospital she excreted 5 liters of urine and during the second 24 hours, 6,245 cc. This patient was fortunate in having a renal mechanism which could handle this load; in an older individual, visceral edema and cardiac decompensation would doubtless have occurred. By the end of 48

hours the patient was waterlogged and well into a period of water retention. She was clinically edematous with a sodium space of 30 per cent of her body weight; hematocrit of 33 and serum protein of 5.2 Gm./100 cc. were further evidences of this dilution. On the third day after the burn she excreted 8,215 cc. of urine in a 24-hour period, an amount larger by 33 per cent than any 24 hour urine output during her entire stay, her edema decreased perceptibly, and the sodium space decreased 6 liters. This can be interpreted only as a spontaneous diuresis of retained water and its occurrence (often discernible only by careful intake-output data) constitutes the best possible prognostic sign from the point of view of fluid therapy in a severely burned patient, though it is not necessarily a portent of survival (cf. Case 268).

In summary this severely burned patient was given intensive fluid therapy, 7 liters more than that outlined on the basis of the extent of her burn. The patient survived because she did not have a primary lung injury producing increased pulmonary capillary permeability and edema, and because she possessed kidneys which could excrete as much as 8 liters of urine in a 24-hour period when called upon to do so by the resorption of the burn edema. It is possible that the patient needed actually less fluid than that outlined by the surface area formula because the excessive therapy may have distended the interstitial space even further.*

TABLE VIII

PLASMA AND EXTRACELLULAR FLUID DATA

Case 231
Male, Age 36, Weight 70 Kg.
Extent of Burn: 68 percent total, 39 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc.	% BW	cc.	% BW	cc.	% BW
1	....	....	32,700	46.5	29,300	41.9
2	....	....	27,000	38.5	28,900	41.3
3	3580	5.1	35,000	50.0		

Case 231.—A 36-year-old male was admitted with burns of 68 per cent total and 39 per cent full thickness. Therapy was administered with great energy in an attempt to avoid shock and oliguria. On the second day post-burn the patient was seen to have massive edematous collections of fluid in his scrotum, buttocks and thighs. On admission he had shown burns of the nares and pharynx and by his second day, frank pulmonary edema was present and the patient was cyanotic. On the third post-burn day a tracheotomy was done in the hope of improving his oxygen exchange. After this the patient regained consciousness only fitfully and died on the 6th day.

During the first 48 hours in the hospital this patient received 32,645 cc. of treatment of which 10,747 or roughly 30 per cent was plasma. This amount of plasma is equal to approximately 20 per cent of his body weight and was over four times his normal circulating plasma volume. It is about 35 per cent more plasma than the volume outlined by the surface area formula. During this time the patient excreted approximately 8 liters of urine leaving him with

* In the experimental animal, the wound volume created by the burn may be slightly increased by an intravenous injection of isotonic sodium solution.[23]

an apparent water retention of about 24 liters. His sodium space expanded to 42 per cent of his body weight and his final thiocyanate space measurement was 50 per cent of his body weight (Table VIII, Chart 1). Too exact an interpretation of such data is not justified but since the expansion was measured at a time when there was generalized edema, the expansion presumably represents a widespread, massive disorder of fluid distribution and perhaps of cell permeability.

At times during the first 48 hours the patient excreted over 900 cc. of urine per hour and the total urine output for the first 24-hour period was 5,671 cc.

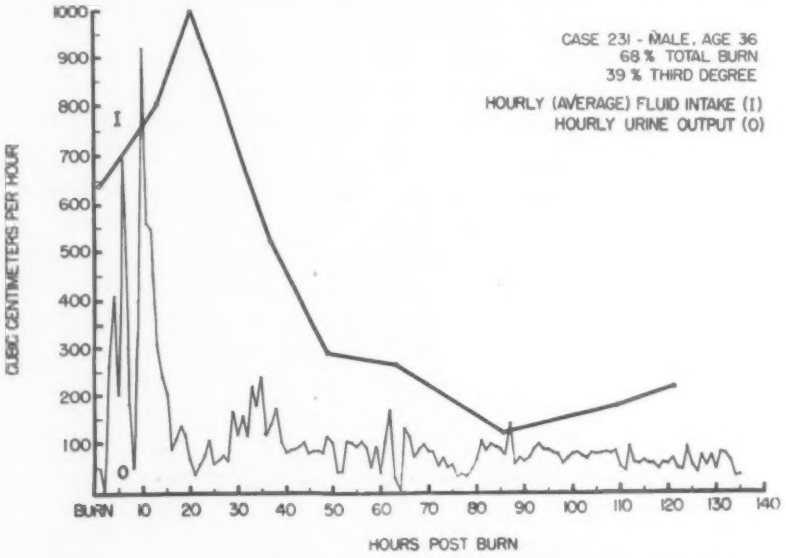

CHART 7.—Intake-Output Chart of an Extensively Burned Patient, Who Received Excessive Therapy and Who Succumbed (Case 231).

Early therapy was administered to the extent of a high urinary output during the first 12 hours. Despite the high output the fluid therapy was further increased until, during the period between 24 and 36 hours, the patient was receiving therapy at a rate approximating 1,000 cc. per hour. Kidney function was unable to keep pace with this tremendous fluid load and the patient developed massive peripheral and pulmonary edema. Therapy was drastically cut at the 40th hour but the patient was unable to diurese the fluid already absorbed and succumbed at the 135th hour.

This output indicates that the patient was being subjected to a water load disproportionate to the actual requirement. However unlike Case 217, who could excrete large volumes of urine consistently for many days, this patient was unable to tolerate so much fluid. His kidneys could not keep up with the therapeutic infusions; the patient never showed any spontaneous diuresis. A direct injury of his pulmonary tract favored the development of intractable pulmonary edema, and death resulted.

In summary, although this patient's therapy was originally outlined on the basis of surface extent injured, the estimate of therapeutic requirement was greatly exceeded because of a clinical impression of the patient's tendency to shock. Huge quantities of fluid were given; the renal mechanism became over-

taxed although the kidneys of this healthy young male were presumably normal prior to burn. The inordinate expansion of extracellular volume was presumably as much the result of excess therapy as of the extensive burn itself.

The events in these last two cases lead to the realization that although patients with extensive burns require massive amounts of fluid therapy in order to compensate for the wound edema, there is a limit to the distensibility of the interstitial space compatible with life. In the first patient, the measured distention of the extracellular fluid volume did not exceed 50 per cent of the normal (Chart 1); the patient survived. In the second patient, the measured distention reached 100 per cent above the normal; the patient died. The safeguard to fluid therapy suggested is that fluid should be restricted to an amount compatible with no more than a 50 per cent increase in the extracellular fluid volume.

The final two patients with extensive burns, both of whom died, are:

Case 234.—A 68-year-old man suffered extensive burns (55 per cent total, 45 per cent full thickness) which proved fatal in nine days. For the first week the patient remained rational. He did not develop visible edema in unburned areas nor did he have

TABLE IX

PLASMA AND EXTRACELLULAR FLUID DATA

Case 234

Male, Age 68, Weight 60.0 Kg.

Extent of Burn: 55 percent total, 45 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc.	% BW	cc.	% BW	cc.	% BW
0 (1 hr.)	....	....	16,500	27.5	15,900	26.4
1	2930	4.9	20,800	35.0	18,000	30.0
2	....	....	23,300	39.0	20,800	35.0
3	2350	4.0	28,800	49.0	19,900	33.0
4	....	....	.....	....	24,300	39.0
5	....	....	24,800	42.0	20,600	34.5
6	....	....	.....	....	19,450	32.5
7	3040	5.0	24,500	41.0		
8	....	....	28,800	48.0	11,260	18.7

pulmonary edema. In his last two days the patient failed gradually and succumbed with clinical evidence of bronchopneumonia and wound infection. Postmortem examination showed bronchopneumonia without alveolar edema, and a chronic nephrosclerosis long antedating the burn.

Fluid therapy was carried out with the intent of avoiding over-administration because of his age and the realization that cardiac decompensation would result if fluid therapy was not carefully restricted. The patient was given less sodium than had previously been the rule and whether as a result of this or of other factors the sodium space was throughout smaller than the thiocyanate space (Table IX). During the last days of his life his thiocyanate space was growing larger while his sodium space was decreasing. This discrepancy coexisted with increasing wound infection.

The patient's therapy was designed to satisfy an extracellular space expansion of approximately 7 per cent of his body weight by the administration of plasma in the first 24 hours, and for this reason he was given 4,800 cc. of plasma in the first 24 hours and a total of 18,000 cc. of therapy. His urine output during this time was 3,500 cc., an amount indicating that the therapy was excessive. During the patient's second 24 hours, treatment was cut down to 7,300 cc., but the urine output was maintained at 1,700 cc. for the 24-hour period, an amount adequate to excrete the normal metabolites. (His non-protein-nitrogen remained normal until his last day.)

Between the second and third days the extracellular space had expanded to 96 per cent above normal, a volume theoretically well in the danger zone of overdistention (Chart 1).

The patient did not live long enough to mobilize any edema; there was no discernible diuresis. It is possible that his renal function was not adequate to excrete the excess body fluid. Death resulted from a combination of factors including wound infection, excessive extracellular fluid which could not be dissipated by his kidneys, as well as age and debility terminating in bronchopneumonia.

TABLE X

PLASMA AND EXTRACELLULAR FLUID DATA

Case 268
Female, Age 83, Weight 60.0 Kg.
Extent of Burn: 62 percent total, 22 percent full thickness

Day	PV		SCNV		Na*V		CL*V	
Post-Burn	cc.	% BW	cc.	% BW	cc.	% BW	cc.	% BW
3	2220	3.7	20,800	35.0	17,670	29.3	10,500	17.5

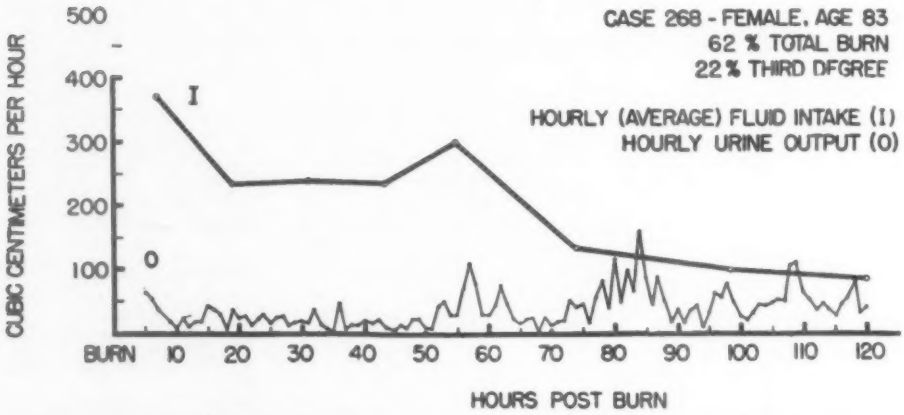

CHART 8.—Intake-Output Chart of an Extensively Burned Elderly Woman Treated with Minimal Quantities of Fluids (Case 268).

With the intent of avoiding overhydration, the intake was kept as low as consistent with a minimally adequate urinary output. In the first 72 hours there is a wide discrepancy between intake and output indicating fluid retention. From the 75th to the 86th hour there is a spontaneous diuresis. Despite the patient's age and extent of the burn there was no pulmonary and minimal peripheral edema.

Case 268.—An 83-year-old female patient was admitted with burns of 62 per cent total, 22 per cent full thickness. Because of her age, fluid therapy, as in Case 234, was given on a limited scale. On the second day she was digitalized. She remained drowsy, became more and more difficult to arouse and uncooperative. Her pulse rate gradually rose and her respiratory rate increased in the last four days reaching a rate of 50. The patient died on the 13th post-burn day with a sudden rise of temperature to 106° and the clinical picture of extensive bronchopneumonia.

Fluid therapy in this patient was carried out according to the scheme that she would require in the first 48 hours plasma amounting to 7 per cent of her body weight (the expected extracellular expansion) plus 1,500 cc. of electrolyte-free water to cover insensible losses, and 1,500 cc. of electrolyte solution to cover kidney function. Her urine output was to be regarded as adequate if it was maintained between 20 and 50 cc. per hour. This regimen was initially successful and although her total urine output during the first

two days of her hospitalization totalled 326 and 515 cc. respectively, the patient did not develop azotemia nor did she show evidences of hemoconcentration.

Justification of this course of systemic fluid therapy appeared on her third post-burn day when with an intake of 2,000 cc. the urine output was larger than that of any previous 24-hour period and she excreted over a liter of urine daily for five successive days. This spontaneous diuresis indicated that she had been able to mobilize her wound edema. On the day prior to her diuresis, an isolated set of volume measurements was carried out, with the intention of checking her therapy (Table X). Her plasma volume was essentially normal. The thiocyanate space was 75 per cent greater than normal, a volume well in the danger zone of over-distention (Chart 1). The sodium space was approximately 3 liters smaller than that of the thiocyanate. A measurement of her chloride space was carried out for experimental purposes (using radio-chloride) and it proved to be 7 liters smaller than the sodium space.

It never was possible to treat her wounds other than by occlusive dressings; extensive wound sepsis culminated in bronchopneumonia and death at the end of two weeks.

The death of both of these patients was influenced by their advanced age and the extensive, infected wounds. Yet it is striking that both had a distention of their interstitial spaces to the degree found in the younger, excessively treated patient who also died (Case 231).

External Water Loss

The loss of water externally from the surface of the wound has been determined in seven patients by measuring the quantity of sodium and of chloride in the exudate (Table XI). The loss is roughly proportionate to the extent of the wound surface, is greatest in the first few days, and diminishes with time. As an average for the first 48 hours, 50 cc. is lost for each 1 per cent of surface area burned. These direct measurements are more accurate than the indirect calculations made in Table III.

Appraisal of Surface Area Formula: Deductions from Observations Thus Far Made

Analysis of the experience gained from the cases described lead us to a statement of nine conclusions concerning the nature of the fluid disorder of thermal burns and to the recognition of two opportunities to improve on the surface area formula for planning the fluid therapy of the extensively burned patient.

1. A relentless expansion of the interstitial fluid volume takes place in the first 36 to 48 hours following a burn. This expansion in the extensively burned patient exhausts the water and protein resources of the plasma and dehydrates the rest of the body if untreated. Inadequate therapy results in renal and other visceral failure.

2. Fundamentally this increase in interstitial fluid volume is the edematous distention in the area of the wound, and the amount of expansion is therefore proportional to the area burned.

3. The proportion is, however, not direct, for as the area burned increases to 30 per cent of the body surface, the expansion of the interstitial space may have already reached a maximum so that the entire extracellular space is 50

per cent above the normal volume (that is, an extracellular space of 30 per cent of body weight). The amount of edema accumulating as the result of a burn to skin depends to some extent upon the specific area burned (face, scrotum and buttocks, for instance, can accumulate more beneath the skin than arms and legs) and upon relocation of this edema from burned to unburned areas (as

TABLE XI

EXTERNAL WATER LOSS CALCULATED FROM EXUDATE SODIUM AND CHLORIDE LOSSES ASSUMING THESE IONS LEAVE THE WOUND AT CONCENTRATIONS FOUND IN EXTRACELLULAR FLUID

Days Post-Burn	Sodium Loss Gm. (Total)	Fluid Loss on Basis of Na cc./Day	Chloride Loss Gm.	Fluid Loss on Basis of Cl cc./Day
	A. Circumscribed Partial Thickness Burn			
	Case 264, 5.5% Burn of Partial Thickness			
0– 3	2.0	153		
	B. Extensive Partial Thickness Burn			
	Case 254, 45% Total Burn, 5% Full Thickness			
0– 4	4.9	375	....	....
5–11	7.8	400	....	....
12–21	5.2	158	....	....
22–31	3.9	119	4.8	131
32–41	4.1	124	3.6	100
42–51	1.5	46	1.2	33
52–61	0	0	0	0
	C. Extensive Full Thickness Burns			
	Case 260, 28% Total Burn, 12% Full Thickness			
0– 4	4.7	360	3.9	265
5–11	12.1	616	9 8	432
12–21	11.7	356	14.4	390
	Case 269, 27% Total Burn, 20% Full Thickness			
0– 4	15.5	1180	17.3	1175
5–11	14.1	720	14.5	660
12–21	27.9	850	40.8	1110
	Case 234, 55% Total Burn, 45% Full Thickness			
0– 4	18.5	1400	....	....
5–11	25.3	1100	....	....
	Case 268, 62% Total Burn, 22% Full Thickness			
0– 4	25.5	1700	30.9	2110
5–11	15.4	1175	18.9	860
	Case 262, 85% Total Burn, 58% Full Thickness			
0– 4	30.7	2350	20.0	1352
5–11	36.8	1870	24.0	1083

for example by gravitation of head edema to the neck and upper thorax). A more extensive surface area burn is not necessarily accompanied by any further expansion.

4. There is a limit to which the extracellular space can expand and the organism survive. An expansion of this space more than 50 per cent over

normal is fraught with danger; the mechanism for disposal of the excess fluid may not be adequate when resorption of edema takes place, and an inordinate expansion of the extracellular measurement in itself indicates widespread changes in permeability.

5. Over-zealous therapy may exaggerate the extracellular space expansion.

6. Renal function is a sensitive index of the balance between tissue thirst, quenching, and over-satiation.

7. External loss of fluid is minor compared with the pooling of edema in the area of the wound, yet it is large enough to be taken into account in therapy. The volume can be estimated on the basis of the area of the wound.

8. Evidence is lacking that pressure dressings materially limit the fluid requirements of the burned patient. Edema fluid is displaced proximally by such dressings.

9. Resorption of edema has started as a rule by the 45th to 50th hour; it may be rapid and overwhelming if fluid therapy is not promptly curtailed.

Although the administration of fluid therapy on the basis of the surface area formula represents a distinct improvement over that based on hemoconcentration, there are shortcomings. The surface area formula does not take into account variation in the volume of edema according to the body area burned and the depth of injury, the relocation of the edema from burned to unburned areas, and the probability that multiple small burns strategically located may overload the lymphatic trunks of one area and lead to a disproportionately large accumulation of fluid. The formula also neglects the complication introduced by damage to the respiratory tract and the factor of size of the patient. Pulmonary damage may increase the requirement for fluid, but it also invites drowning. As for the size of the patient, it is obvious that there is more edema beneath 1 per cent of the skin of a large man than 1 per cent of a small woman or child. But the most important shortcoming of this formula is the absence in it of any idea of restraint. On the contrary, there is in it a temptation to over-estimate the extent of the area burned. Our difficulties have resulted from over-zealous treatment.*

Since the interstitial space expansion can be predicted, the needs of the patient can be satisfied by basing therapy on the anticipated expansion, both in volume and in time. Such an approach might make up for the deficiencies of the surface area formula; it should insure adequate therapy in patients with burns of 30 to 50 per cent of the body surface and restrain over-zealous treatment in patients with burns of 60 to 100 per cent. It would tend to limit the amount of fluid which must be excreted once resorption starts. The observations that the three of our patients whose extracellular fluid volume expanded more than 50 per cent over normal died, and that renal function is a sensitive index of the state of hydration, lead to the concept that both the anticipated interstitial space expansion and renal function could be used in planning and guiding therapy.

* Dr. D. W. Richards, Jr., has also emphasized the importance of avoiding excessive fluid therapy in the extensively burned patient.[28]

Formula Based Upon Anticipated Interstitial Space Expansion

The following formula, based on the anticipated interstitial space expansion, is suggested for the fluid therapy during the first 48 hours of the patient burned 30 per cent or more of the body surface:

Fluid is to be given to replace that lost in four ways: as (1) wound edema, (2) from the wound surface, (3) urine and (4) insensible water. The first two are wound fluid, in composition the same and are logically therefore considered together. The protein concentration of this fluid is approximately 4 per cent, two-thirds that of plasma, while the electrolyte content and concentration equal that of plasma.*

In the first 48 hours the following amounts are to be given:

1. For wound edema, a volume equal to 10 per cent of the body weight.

2. For external loss an amount varying according to the area of wound surface:

Burns of 25–35 per cent	= 1,000 cc.
35–60 per cent	= 2,000 cc.
60 per cent and over	= 3,000 cc.

Add 1 and 2; two-thirds of this combined volume is given as plasma and one-third as non-colloid isotonic electrolyte solution. This 48-hour ration is divided into four equal parts; two parts are scheduled for the first 12 hours, one part for the second 12, and the fourth part for the second 24-hour period. This rationing, weighted in the first 12 hours, takes into account the fact that the redistribution of fluid occurs most rapidly in the initial hours after injury. The time intervals are, of course, calculated from the time of burn and, if the patient enters six hours from the time of burn, the subsequent six hours must include the administration of the full 12 hours' ration.**

3. For renal excretion, 1,500 cc. for each 24 hours, 3,000 cc. total, of non-colloid fluid. One-half is to be given as isotonic electrolyte intravenously. The other half as glucose in water if given intravenously or as palatable fluids if by mouth.

4. For insensible loss, 1,500 cc. for each 24 hours, 3,000 cc. total, of non-colloid, non-electrolyte solution, glucose in water if given intravenously, or palatable low salt fluids if by mouth.

It would be unreasonable to expect this formula alone to suffice for clinical care because hourly alterations in rate of water-transfer and excretion occur; insensible and surface losses are at best estimates and the water resulting from

* The protein concentration of the wound fluid is described in the following paper.[27]

** For example, in a 70 kg. man with 50 per cent of his body surface burned the volumes for the first 48 hours would be as follows:

10 per cent body weight	= 7,000 cc.
External loss	= 2,000 cc.
Total	9,000 cc.
Two-thirds as plasma	= 6,000 cc. plasma
One-third as saline	= 3,000 cc. saline

This 9,000 cc. is to be given in the time schedule outlined in the text.

metabolism is variable. As with the surface area formula, there is need for a sensitive and significant means of following the clinical progress of the patient.

Renal Output as Adjunct to Plan of Therapy

As experience accumulated it became evident that our previous methods of evaluating the day to day or hour to hour course of a burned patient were not wholly satisfactory. Hematocrit provided a measure of inadequate plasma therapy; if it remained consistently over 55, shock and oliguria resulted. Between this and the production of hemodilution and edema by over-administration of fluid there remained a wide area in which hematocrit, plasma protein concentration and body space measurements were poor guides. If one administered treatment until the hematocrit fell into the thirties, it was already too late to remedy the serious waterlogging evidenced by the hemodilution.

The simplest index of the state of balance between needs and therapy that we could discover was an hour to hour vigil over renal output. This was provided by placing an inlying catheter in the bladder, letting it drain by gravity into a small vessel, and recording hourly the amount and specific gravity of the urine. The value of this maneuver in Case 149 has already been described in detail. Charts based on the average intake and output of other cases whose problems have already been discussed are shown in Charts 3 through 8. These quantitative urine output data in general indicate three types of situations commonly encountered in which the usefulness of this method was most readily apparent:

Adequate hourly outputs in the normal to high range (50 cc. or more per hour up to 200 cc. per hour) bespeak the adequacy of therapy and warn against increasing fluid intake.

A falling or low hourly output (30 cc. per hour down to 5 cc. per hour for three hours or more) calls for immediate increase of therapy, a necessity not evident for many hours if the hematocrit alone is used. The earlier the low urine output appears after the burn, the more pressing the need for increased therapy.

Hourly urine outputs over 200 cc. per hour for more than six hours signify over-treatment if encountered in the first 48 hours or spontaneous diuresis if after the 48th hour. This hourly volume calls for a drastic cut in fluid administration if one is to avoid plethora, pulmonary edema or congestive heart failure.

There was one finding, however, which was equivocal, using the hourly urine output as an index of therapy. This was a continued low output (0 to 30 cc. per hour) for many hours in the face of continuing therapy. Under these circumstances two opposite explanations offer themselves, and it is of the greatest importance to distinguish between them:

1. The therapy underway may be inadequate, or

2. A renal lesion is present (due to anoxia,[26, 29] dehydration, hemoglobinuria[30, 31, 32] or damage antedating the burn) which renders more output impossible, and in the face of which any increase in therapy is even more apt to produce edema and heart failure.

The differentiation of these two fundamentally different causes for the oliguria can be accomplished by administering 1,000 to 1,500 cc. of fluid rapidly by vein (40 to 60 minutes), a procedure termed the water tolerance test. This amount of infusion has not been deleterious in our experience if not continued over 60 minutes. It may constitute but a small fraction of the day's intravenous ration. The renal response is most significant. If a clear-cut increase in hourly urine output occurs, one may conclude that the kidney is able to handle the water but that the wound demand is not being met by the previous course of treatment. On the other hand, if there is no renal response, one should exercise considerable caution in continuing intravenous therapy on an extensive scale.

The exact nature of the fluid administered for the water tolerance test depends to some extent on the situation in which the patient is found. In most of the instances in which this type of infusion has been used to test kidney function we have used a 5 per cent solution of dextrose in distilled water. In one or two patients in whom salt had purposely been restricted because of age or preexistent cardiac disease, the possibility existed that oliguria represented a salt deficit as much as a water deficit and for this reason the water tolerance test infusion has consisted of normal saline. In one patient (Case 149) therapy was over-weighted with non-colloid-containing solutions at the time that the oliguria occurred and he also showed severe hemoconcentration with respect to red cells; it was clear that the test infusion should consist of plasma.

In any case the infusion is run in so rapidly that a transient plasma volume change is produced regardless of the infusing material. The use of plasma for such a water tolerance test should be approached with caution because, in the absence of a plasma deficit, cardiac embarrassment may be produced, even in the absence of overt myocardial disease.

Trial of the Volume Expansion Formula and Renal Function Guide

Since the fluid therapy of burned patients is a problem only in the extensively burned, trial of the new plan of therapy, based on the anticipated increase in volume of the interstitial space and refined by attention to the renal function, was made upon patients with such burns. Five cases have been selected with full thickness burns who were so treated and in whom adequate measurements of water balance were made to permit comparison of the method with that of the surface area formula. There were two fatalities; both patients had respiratory tract injury. Only one patient had early excision and grafting of the full thickness wounds. Since the importance of these cases lies in the details of their care and response, they are presented separately.

Case 260 (Chart 9).—A 27-year-old tuberculous woman received burns of 28 per cent total, 12 per cent full thickness. The burns were distributed around the trunk and arms with some areas on lower abdomen, buttocks and legs. After the initial phase of fluid imbalance had been controlled, on the 9th post-burn day the critical areas in axilla and popliteal space were excised and grafted. Healing elsewhere was gradual and she was discharged on the 94th day.

By plan she was to have received 5,500 cc. of plasma, 5,500 cc. of saline for wound

dilution and external loss (an overestimate of saline), 2,000 cc. of saline for urine output, and 3,000 cc. of dextrose in water to cover lung losses in her first 48 hours. This scheme was not adhered to, as her plasma totalled only 3,650 cc. in the first 48 hours (plus one whole blood transfusion). Her saline, at 7,100 cc., was essentially that outlined. The water (electrolyte-free) intake totalled 5,600 cc. During the first 48 hours she lost 1,545 cc. as vomitus and could take nothing effectively by mouth.

By 10 to 12 hours after injury, her urine output had dropped to 0 to 25 cc. per hour and her intravenous intake was therefore accelerated, and for two hours she received a rapid infusion (approximately 1,000 cc. per hour) of 5 per cent glucose in water (Chart 9). This was followed by a rise in urine output to 400 cc. per hour indicating that her previous rate of infusion was too slow. Her maximum hematocrit of 52 per cent just previous to the water tolerance test dropped to 44 per cent the next day.

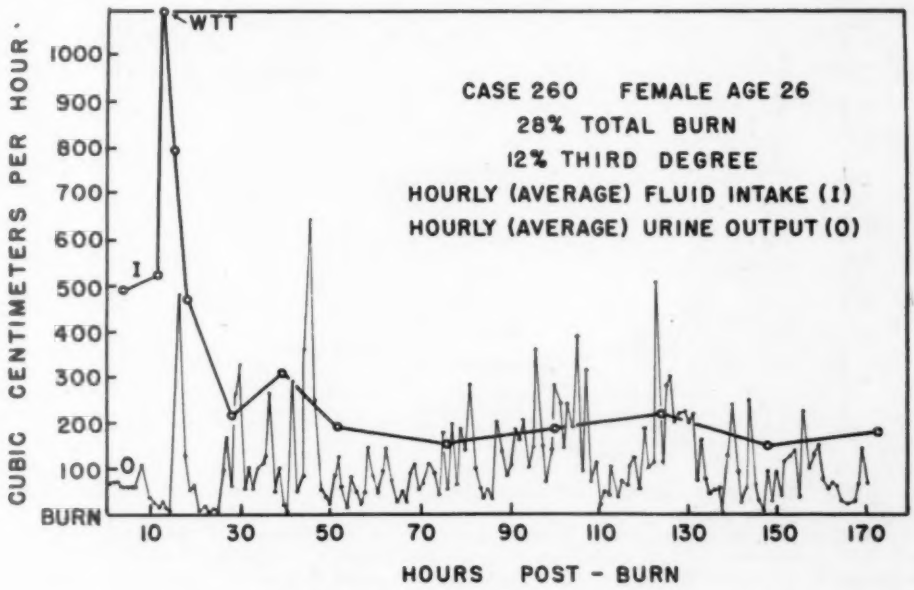

CHART 9.—Intake-Output Chart of a Patient with a Total Burn of 28 Per Cent Demonstrating the Use of the Water Tolerance Test (Case 260).

Therapy was begun and a customary intake-output discrepancy was observed as one would expect in a burn of this magnitude. At the 10th to 14th hour, urine flow practically ceased. Therefore, a rapid infusion was begun and there was a gratifying response in urine output, indicating that the needs of the wound were not quite being satisfied by the earlier therapy. As soon as this rapid infusion was stopped, however, urine flow again fell to a low level and therapy should have been increased. At 30 hours the patient responded with a spontaneous diuresis, indicating that the peak of edema formation was approaching and that the period of oliguria had not been long enough to produce renal damage. Had the two periods of low renal output occurred several hours earlier, when the rate of edema formation presumably was at its height, the failure to increase the rate of fluid therapy following the water tolerance test might have been followed by renal damage.

Case 262. (Chart 10).—A 64-year-old Portuguese male admitted 10 hours after sustaining burns covering 85 per cent of his body surface. Fifty-eight per cent was of full thickness destruction, some of it deeply charred. His course was steadily downhill after the fourth post-burn day; he coughed up blood-tinged sputum and died of respiratory failure with respirations up to 70 per minute on his 8th post-burn day. Postmortem examination showed generalized arteriosclerosis, an hemorrhagic pulmonary lesion, nephrosis and nephrosclerosis.

On admission the patient showed hemoconcentration with an hematocrit of 65 per cent and plasma protein of 7.7 Gm./100 cc. His estimated body weight was 60 kg. Because of the 10-hour lapse and presence of established shock the fluid ration was heavily concentrated in his first 12-hour period.

The expansion formula was followed and in his first 12 hours he received 4,250 cc. of plasma, 5,000 cc. of other intravenous fluids (3,000 of which were saline) and one whole blood transfusion. His response to this was gratifying. He rallied clinically, his urine output rose from near zero levels to 100 cc. per hour and in the next 12 hours to 200 cc. per hour (Chart 10). His hematocrit fell to 40.2 per cent and his non-protein-nitrogen to 48 mg./100 cc. (from a level of 55 mg./100 cc. on admission). By his 40th hour, urine output was sufficient to justify lowering his intake to less than 200 cc. per hour and despite this he maintained good urine output, indicating a tendency to diurese his edema.

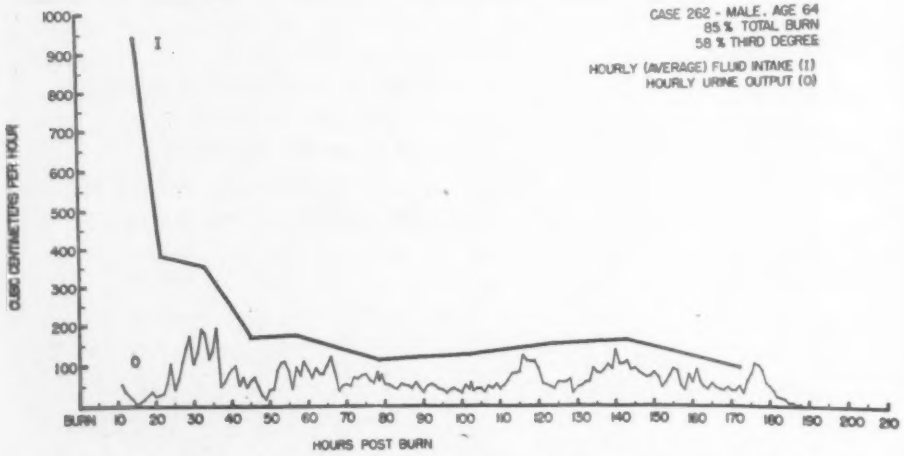

CHART 10.—Intake-Output Chart of an Elderly Man with a Burn of 85 Per Cent Who Succumbed (Case 262).

An early high intake-output discrepancy indicates the amount of fluid required to satisfy the demands of the wound in this patient before a satisfactory urinary output appeared at the 23rd hour. Thereafter, intake was cut down to a level adequate to maintain normal urine flow until 185 hours post-burn at which point the patient became oliguric despite therapy and died. Postmortem examination showed preexisting renal disease in addition to extensive wounds.

From this point on, however, he failed to improve; his non-protein-nitrogen remained elevated and terminally, with a temperature of 104, pulse rate of 160 and respiration rate of 70, anuria developed, preceding death by three or four hours. The terminal events were those of respiratory tract burn, evidenced on admission by burn of the nares and pharynx and leading to cyanosis, pulmonary exudate and death.

Case 269 (Chart 2).—A 60-year-old luetic alcoholic was admitted 22 hours after receiving burns totalling 27 per cent with 20 per cent full thickness. On admission the patient was in borderline circulatory failure with an hematocrit of 59 per cent which, during the first 12 hours of therapy, fell to 52 per cent, and then dropped to the range of 38 to 42 per cent where it remained for a week.

Because of the 22-hour lapse before therapy, and despite the elevated hematocrit, he was given a whole blood transfusion initially. By plan he was to receive 3,000 cc. of plasma in his first 12 hours in the hospital, with lessening amounts thereafter. It was hoped that a water intake of 2,500 cc. could be attained orally in his first 12 hours. If not, suitable intravenous supplement was planned. This plan was adhered to and he received

4,200 cc. of plasma in his first 32 hours in the hospital in a total treatment regime of 16,000 cc. of which 5,300 cc. were orally administered.

Urine flow almost ceased from the 27th to the 32nd hours (Chart 2). A water tolerance test was given which was followed by a diuresis lasting for nearly 12 hours. This diuresis indicated that the earlier therapy had been more nearly adequate than suggested by the low urinary output.

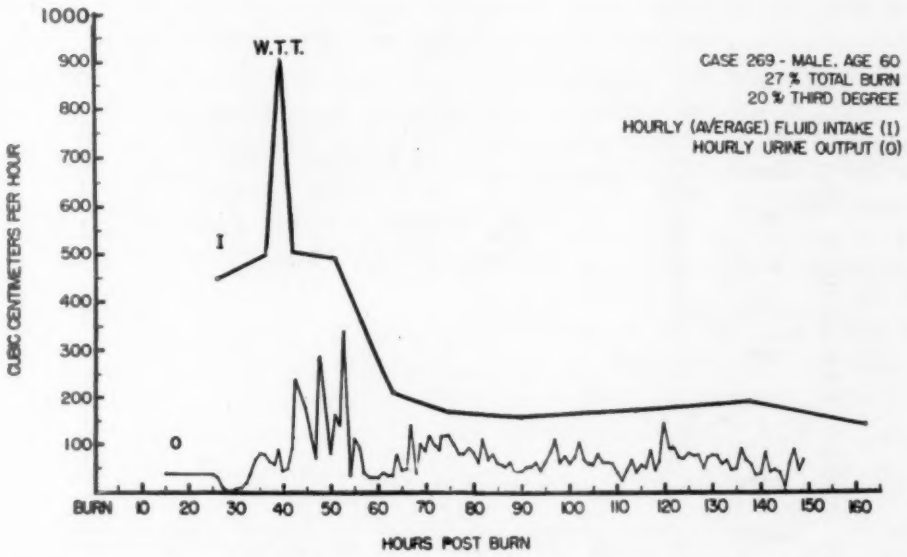

CHART 11.—Intake-Output Chart in a Patient with a Moderately Severe Burn Demonstrating a Response to the Water Tolerance Test at 40 Hours, Administered Because of Low Output Rates in the Previous Eight Hours (Case 269).

An obvious diuresis was produced which lasted almost 12 hours, indicating that the demands of the wound had previously been met more satisfactorily than revealed by the earlier transient low urinary output.

Case 280.—A 40-year-old feeble-minded male was brought to the hospital within three hours after receiving burns of a total of 58 per cent, 45 per cent estimated as full thickness. There were obvious burns of nose, pharynx and larynx. Seven hours after entry a tracheotomy was done. He died seven days after entry with evidences of pulmonary tract burn as the chief cause of death. Three days before death, laryngoscopy showed necrosis of hypopharynx, epiglottis, esophageal orifice and larynx as far down as could be seen.

The plan called for 20,000 cc. in 48 hours, half of this in the first 12 hours. This plan was not strictly adhered to because of an adequate renal output with slightly lesser amounts of therapy, and in the first 18 hours he received but 3,000 cc. of the 5,000 cc. of plasma planned. (This demonstrates the flexibility of the hourly urine output technic and the ease with which a decrease in ration may be adjudged safe.) His kidneys put out 25 to 180 cc. per hour, averaging 100 cc. per hour during this time. Because of this, a diminution in ration was adopted and despite his airway burn, the patient did not develop pulmonary edema and maintained an excellent tracheotomy airway and tidal volume until 24 hours before death, when obstruction due to necrosis in the trachea developed.

Case 281 (Chart 12).—A 26-year-old woman entered the hospital because of burns of 32 per cent total, 25 per cent full thickness. The right arm was so deeply burned that on

the 8th day amputation at the mid-forearm became necessary with excision of the burns of the remainder of the arm. The grafts took satisfactorily, but 13 days after the initial amputation, reamputation through the mid-humerus was necessary because of sepsis in the elbow joint. From then on the patient's course was uneventful.

The plan of treatment included 5,000 cc. of plasma, 3,000 cc. of saline and 2,000 cc. of glucose in water for the first 48 hours. This regimen was followed, but the morning following the burn the hourly urine output was continuing low (10 to 15 cc. per hour for 3 hours) and, therefore, a water tolerance test was performed (Chart 12). A response

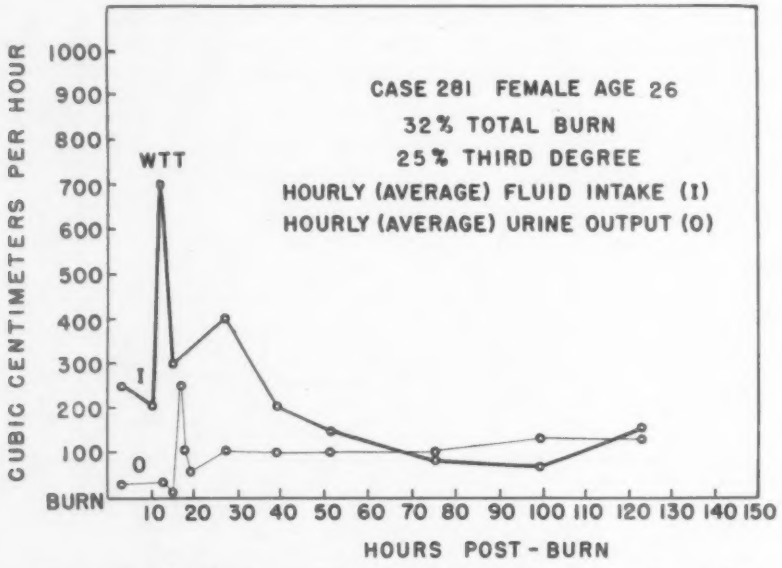

CHART 12.—Intake-Output Chart in a Patient with a Deep Burn of the Upper Extremities Requiring Amputation (Case 281).

Response to a water tolerance test given at the 12th hour post-burn indicated the need for more intensive therapy, which was accordingly given. At the 40th hour the intake and output relation was normal. From the 70th to the 115th hours, the output exceeded the intake pointing to resorption of wound edema.

with an output of 250 cc. for the first hour, then 110 and 90 cc. showed that kidneys could function satisfactorily if provided with enough fluid; the intravenous ration was increased, renal function remained optimal from then until healing.

The patient had a spontaneous diuresis on the second post-burn day when, with a sharp fall in intake, the urine output was maintained and then gradually rose. This diuresis was presumably occasioned by beginning resorption of wound edema.

SELECTION OF FLUID FORMULA

By what formula shall the fluid therapy of the extensively burned patient be guided in the first days after injury? For normal-sized adult patients, burned up to 50–60 per cent of their body surface, the surface area formula, guided by the renal output, is a safe and sufficient method of planning the fluid therapy for the first 48 hours; for more extensive burns or in patients of unusually large or small habitus, the formula may be misleading. In patients whose burn is 30 per cent or more, the expansion of the interstitial portion of

the extracellular space may become maximal, and the formula based on expected extracellular space expansion will also apply satisfactorily. It, too, should always be used in conjunction with the renal output guide. Whichever formula is used, one must not hesitate to depart from plans and admit errors in prediction if the kidneys protest.

After 48 hours, with either formula, a regimen similar to the second 24 hours is maintained until the kidneys indicate the onset of diuresis and fluid therapy is immediately curtailed. At this point a shift over to controlled and restrained oral intake may often be made. In patients with burns predominantly of partial thickness, the diuresis appears promptly and may be massive since resorption of edema may proceed at a pace almost the equal of formation. In patients with burns of full thickness destruction the resorption of edema is slower and the diuresis therefore less pronounced. The hourly urine figures are usually no longer useful after the 8th day, though in occasional cases there may be disquieting periods of oliguria up to 14 days and the urine chart should then be maintained.

During this early period there are many other important considerations such as caloric and vitamin intake, nitrogen intake, red cell replacement, sedation, tracheotomy, chemotherapy, etc.* The outlines of therapy cover only fluid therapy; the other features are dealt with elsewhere.

SUMMARY

The extracellular space has been measured in a series of burned patients, patients with other diseases and normal human beings, dehydrated and given therapy. The measurements have included the plasma, thiocyanate and radiosodium volumes.

Almost identical in normal individuals, the radiosodium and thiocyanate volumes may differ in burned patients. In the first days after injury, the radiosodium may be the larger. In the later days, concomitant with wound infection, the thiocyanate volume surpasses that of the radiosodium. These discrepancies point to differential cell permeabilities for the two ions.

In the burned patient an expansion of the extravascular extracellular space or interstitial space is the important feature of the disordered fluid balance; though there is external fluid loss from the wound, the interstitial space is, nonetheless, the chief recipient of plasma loss. Pressure dressings do not effectively limit the interstitial space expansion.

Therapy must be planned to satisfy, and not augment, this pool of wound edema. Over-treatment will exaggerate the defect and in the extensively burned patient will endanger survival.

Measurement of the hourly urine output is the most ready means of checking the adequacy or noting the excess of treatment.

* The necessity of special nursing and a professional visit at intervals of only a few hours is obvious from the nature of the measures taken to insure success. The care of an acute burn can, from the point of view of professional care needed, best be compared to diabetic coma or advanced tetanus.

A simple water tolerance test is described which allows a more accurate interpretation of small hourly urine outputs.

All of the fluid needed to prevent circulatory failure and dehydration of the body in the first 36 to 48 hours must eventually be excreted by the kidneys or exhaled by the lungs, if not lost in the exudate. When resorption of edema is manifest after the 48th hour, fluid therapy must be promptly curtailed to avoid pulmonary edema. In burns of partial thickness the resorption may proceed almost as rapidly as the formation while in those of full thickness destruction the resorption is generally slower.

The practical application of this knowledge to extensive burns is described. Plans of therapy, based upon the anticipated expansion of the interstitial space as well as the surface area burned, are outlined for patients having a burn of 15 per cent or more of the body surface.

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OF NEMBUTAL'S CLINICAL USES

SEDATIVE

Cardiovascular
Hypertension[1]
Coronary disease[1]
Angina[1]
Decompensation
Peripheral vascular disease

Endocrine Disturbances
Hyperthyroid
Menopause—female, male

Nausea and Vomiting
Functional or organic disease (acute gastrointestinal and emotional)
X-ray sickness
Pregnancy
Motion sickness

Gastrointestinal Disorders
Cardiospasm[2]
Pylorospasm[2]
Spasm of biliary tract[2]
Spasm of colon[2]
Peptic ulcer[2]
Colitis[2]
Biliary dyskinesia

Allergic Disorders
Irritability
To combat stimulation of ephedrine alone, etc.[3,1]

Irritability Associated With Infections[4]

Restlessness and Irritability With Pain[3,4]

Central Nervous System
Paralysis agitans
Chorea
Hysteria
Delirium tremens
Mania

Anticonvulsant
Traumatic
Tetanus
Strychnine
Eclampsia
Status epilepticus
Anesthesia

HYPNOTIC
Induction of Sleep

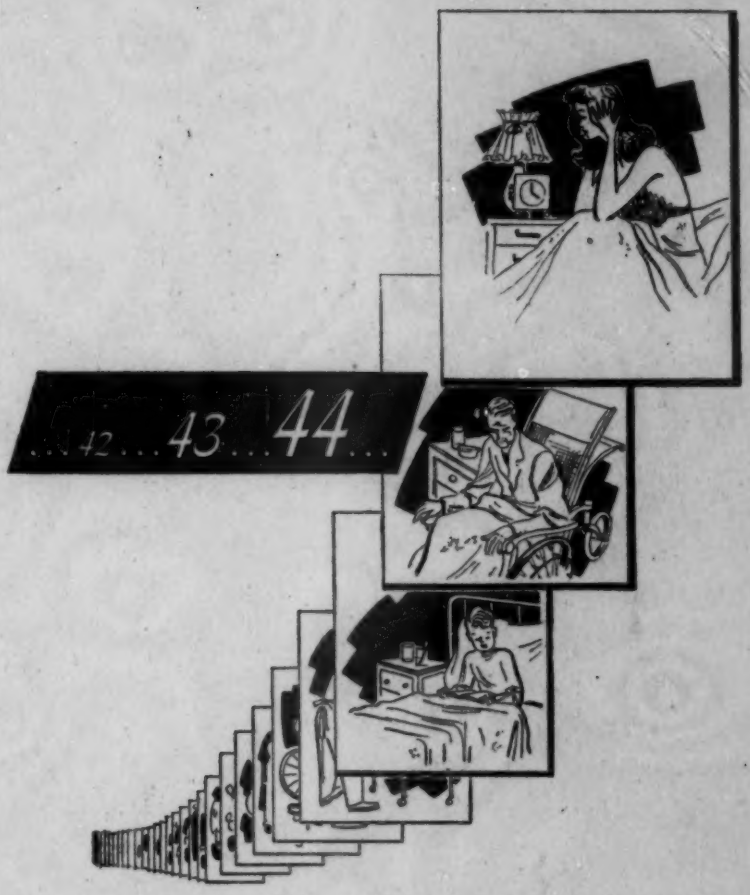
OBSTETRICAL
Nausea and Vomiting
Eclampsia
Amnesia and Analgesia[5]

SURGICAL
Preoperative Sedation
Basal Anesthesia
Postoperative Sedation

PEDIATRIC
Sedation for:
Special examinations
Blood transfusions
Administration of parenteral fluids
Reactions to immunization procedures
Minor surgery

Preoperative Sedation

Nembutal alone or [1]Glucophylline® and Nembutal, [2]Nembutal and Belladonna, [3]Ephedrine and Nembutal, [4]Nembutal® and Aspirin, [5]with scopolamine or other drugs.



Yes, more than 44 clinical uses for short-acting Nembutal (see list at left) have been reported in the literature. Published articles—now in the hundreds—prove that Nembutal efficiently fills any short-acting sedative or hypnotic need. Depending on the purpose, the dosage can be controlled so that any degree of cerebral depression—from mild sedation to deep hypnosis—is possible. Furthermore, the dosage required is small—about half that of many barbiturates. Thus your patient receives the benefits of shorter effect, less drug to be inactivated, marked clinical safety, less possibility of barbiturate "hangover"—and prescription economy. These outstanding qualities may suggest that you widen your field of Nembutal application. Your pharmacy will be pleased to supply you with any of eleven different Nembutal products in convenient small dosage forms. ABBOTT LABORATORIES, North Chicago, Illinois.

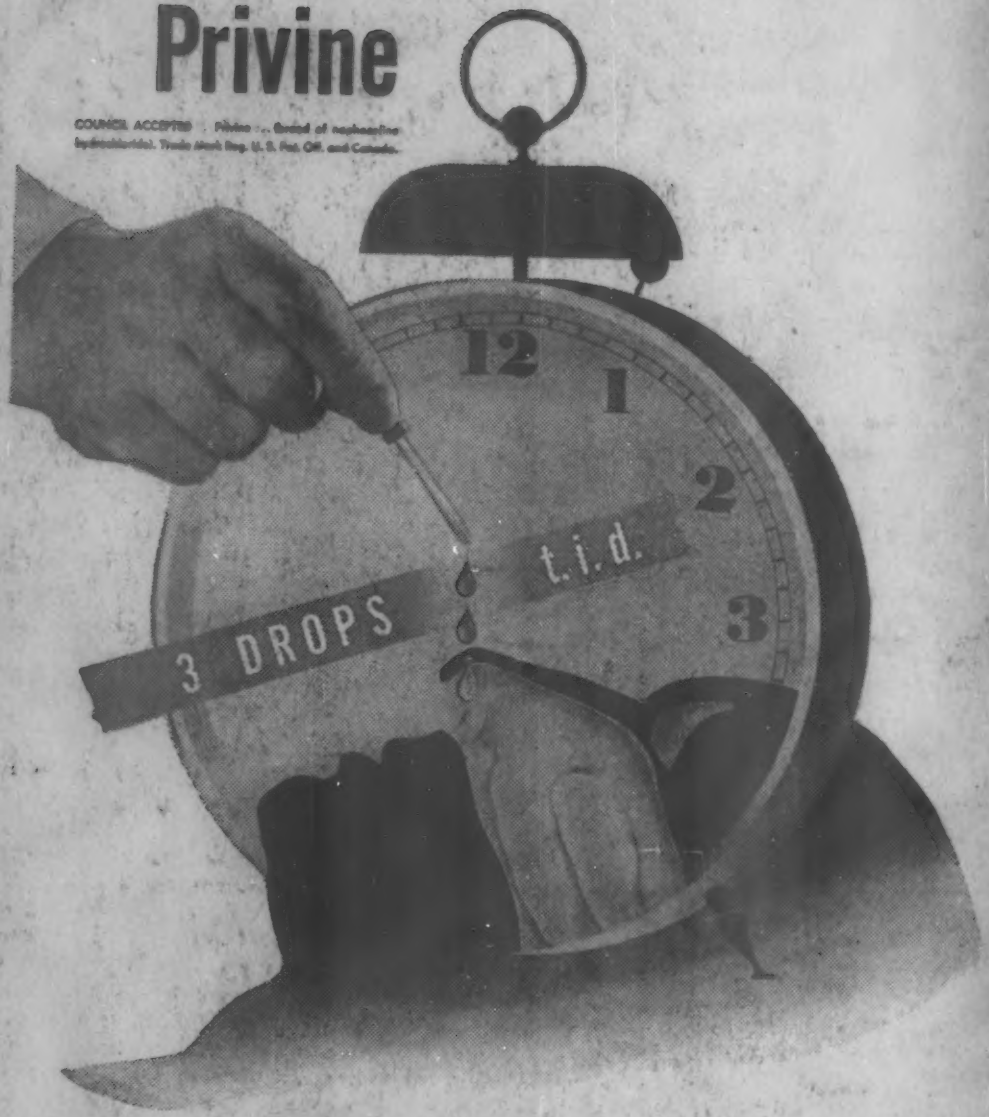
In equal oral doses, no other barbiturate combines QUICKER, BRIEFER, MORE PROFOUND EFFECT than

Nembutal®

(Pentobarbital Sodium, Abbott)

Privine

COUNCIL ACCEPTED · Privine · ... Brand of naphazoline hydrochloride. Trade Mark Reg. U. S. Pat. Off. and Canada.



So effective is this widely prescribed vasoconstrictor that three drops, in each nostril, t.i.d. are sufficient to provide rapid, prolonged relief. Also available in convenient jelly form.

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